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A COMPARISON OF ORAL CHOLECYSTOGRAPHIC FINDINGS AND PROVED EVIDENCES OF GALLBLADDER DISEASE*

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ELEVEN years have elapsed since the appearance of the communication by Graham and Cole[1] concerning the roentgen visualization of the human gallbladder following the intravenous administration of halogenated phenolphthalein compounds. During that period a truly impressive number of publications has accumulated dealing with this subject and others more or less directly related. One emerges from a perusal of this literature with a clearer understanding of the physiology of the biliary apparatus as well as a quickened interest in the clinical manifestations of the disease processes which may affect it. Judging from the many published reports regarding the accuracy of cholecystography in recognizing dysfunction of the gallbladder as controlled by surgical and pathological methods, it may be assumed that this diagnostic procedure is highly dependable. Shortly after oral administration of the dye came into widespread use, sharp differences of opinion were voiced by various writers regarding the relative reliability of that technique as opposed to the originally described intravenous administration. However, the published figures of Kirklin[2,3,4] and Graham,[5] both widely quoted by others, indicate that satisfactory results may be confidently expected following either type of dye administration, providing technical details are faithfully observed.

During the past two years Potter-Bucky diaphragms have been developed capable of sufficiently high speed travel to permit the use of exceedingly short exposures of the order of one-twentieth of a second. Since rapid exposures are distinctly advantageous in order to prevent motion of the gallbladder during exposure, this mechanical development may lead to even greater accuracy than has in the past been reported. Stewart and Illick[6] have introduced a method of oral administration the chief feature of which is the maintenance of high concentration of dye in the blood stream for a longer period than was the case in the originally recommended oral technique. It is claimed that this method of reinforcement of dye concentration in the gallbladder results in fewer false reports of non-visualization.

When the gallbladder can be clearly and distinctly visualized after dye administration with no sign of included stone within its contours, one feels a comfortable degree

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of confidence in reporting to the referring physician the absence of any sign indicative of gallbladder dysfunction. When gallstones, be they densely opaque, partially opaque, or visible only as defects in the dye shadow, can be unequivocally recognized, an even greater degree of confidence is justifiable. Although published figures

TABLE I

TWO YEAR PERIOD

April 1, 1932 to April 1, 1934

Cholecystographic examinations (oral method)	2,781
Excluding 112 indeterminate and unsatisfactory examinations	2,669
Number of cases	2,505
Cases with one examination	2,356
Cases with two examinations	134
Cases with three examinations	15

indicate that complete absence of a gallbladder shadow, technical procedures being rigidly controlled, is more reliable than any other single observation, one is apt to find a certain reluctance on the part of clinicians to rely greatly upon this roentgenological sign. Unless clinical symptoms and signs very strongly support roentgen evidence of biliary dysfunction, physicians are apt to attach great weight to the probability of technical error when the gallbladder fails to become visible. With the desire to determine the diagnostic value of cholecystography as carried out in this institution, a survey was begun of two years' experience with oral cholecystography at the University Hospital, University of Michigan. This survey concerns the 2,781 oral cholecystographic examinations conducted in the Department of Roentgenology during the two year period ending March 31, 1934. Of these, 112 were reported as indeterminate or otherwise unsatisfactory and have therefore been omitted from this study, leaving a total of 2,669 examinations representing the study of 2,505 patients (Table I).

Although 1,075 patients were reported as showing some form of gallbladder abnormality as the result of cholecystographic examination, only 203, or slightly less than 20 per cent, were subjected to surgical proof or were subsequently observed at autopsy. Although there are many reasons why roentgenological evidence of biliary dysfunction does not and should not constitute an indication for surgical intervention, it is, nevertheless, disappointing to learn that the opportunity to gauge the accuracy of cholecystographic observations is not available in a greater percentage of all cases in which evidence of dysfunction was reported. The opportunity to observe the gallbladder status at operation and the autopsy table in the case of those patients reported as showing normal function was still further limited; only 35, or 2.4 per cent, of the 1,430 cases so reported being later subjected to proof. One is forced to remember in drawing conclusions from those instances in which proof is available that the bulk of his observations, at least in this field of roentgen diagnosis, are destined to remain unverified, except so far as clinical symptoms and signs may support or contradict (Table II).

TABLE II

DISTRIBUTION OF CASES ON BASIS OF ROENTGEN DIAGNOSIS

	All Cases	Proved Cases	
Normal visualization without stone	1,430	35	2.4%
Normal visualization with stone	109	18	16.5%
Non-visualization without stone	654	120	18.3%
Non-visualization with stone	81	32	39.5%
Faint visualization with and without stone	231	33	14.2%
Total number of cases with proof		238	9.5%

TECHNICAL METHODS

The technique employed in this department may be summarized briefly as follows: Patients are supplied with printed instructions and a prescription drawn on the hospital's pharmacy at the time they are given an appointment for examination. The printed instructions call for omission of fat and meat from the evening meal and

the ingestion of 6 ounces of a prepared dye solution during the course of this evening meal. The patient is further instructed to retire early and to abstain from further ingestion of food or drink of any sort until after his examination in the roentgen department. The prepared dye solution supplied by the pharmacy consists of 4 grams of Mallinckrodt tetraiodophenolphthalein crystals thoroughly dissolved in 2 ounces of distilled water and mixed with 4 ounces of blue grape juice. If shaken before drinking, this mixture is homogeneous and no settling of undissolved dye occurs.

Between the hours of eight and nine the following morning, approximately fourteen hours after dye ingestion, the patient reports for roentgen examination. He is placed prone on the examining table, the right hip is elevated very slightly with a sand bag, and two exposures are made with grid technique at 36 inch distance, 50 milliamperes, $1\frac{1}{4}$ seconds' exposure. The only variable factor, voltage, is determined by the thickness of the patient. The first of these two exposures is made on an 8″ by 10″ film to include the tenth to twelfth ribs, a portion of the vertebral column, and the entire course of the abdominal margin laterally. The second exposure, also on 8″ by 10″ film, is made to include a generous portion of the wing of the ilium. This procedure insures two separate poses of the patient and minimizes the likelihood of failing to record an otherwise visible gallbladder shadow because of movement or unusual position in the abdomen.

As soon as this preliminary filming is completed the patient is given 2 ounces of milk and 2 ounces of cream thoroughly mixed, and within the succeeding hour the filming process is repeated in order to take advantage of the customary increase in density of the gallbladder shadow and to assist in the recognition of stones by virtue of their altered relationships within the narrowed lumen of the gallbladder after partial emptying.

All gallbladder roentgenography is carried out in one particular exposing room and with but few exceptions all exposures are carried out by the same technician. As a matter of routine, this technician inquires of every patient regarding his reaction to the dye and records on the requisition sheet whether or not the patient retained the dye and, if not, at what period after ingestion vomiting occurred. In reporting cholecystographic findings, due allowance is made for these notations, and if vomiting has occurred within the first thirty minutes non-visualization is discounted pending re-examination. Cholecystographic findings in this series were reported over the two year period by a group of nine roentgenologists. The bulk of the reports, however, came from one observer.

Following the plan suggested by Kirklin, response to the cholecystographic test was uniformly reported by one of the following statements:

1. Normal visualization without stone.
2. Normal visualization with stone.
3. Faint visualization without stone.
4. Faint visualization with stone.
5. Non-visualization without stone.
6. Non-visualization with stone.

VERIFICATION OF ROENTGEN OBSERVATIONS

In analyzing this material, mechanical sorting equipment was used which greatly facilitated study from numerous viewpoints, since it was possible to list upon individual punch cards for each patient detailed data later sortable in a great variety of ways. Proof as to the correctness of roentgenological observations was drawn from the following sources:

1. Subsequent observations at laparotomy regarding color and pliability of the gallbladder, presence or absence of palpable stones in the gallbladder or in the biliary ducts, and the presence or absence of multiple adhesions about the gallbladder.
2. Reports submitted by the Department of Pathology based on the

microscopic appearance of biopsy material removed at operation.

3. Similar reports from tissue obtained at subsequent autopsy.

Dr. Carl V. Weller, Director of the Department of Pathology, very kindly drew up the following classification of microscopic findings, in keeping with which all available data were tabulated (Table III).

TABLE III

CHARACTER OF PATHOLOGICAL PROOF

Classification of Microscopic Pathology

I. Essentially normal	
II. Minor inflammatory disease	Without stone With stone
III. Major inflammatory disease	
(a) Essentially latent	Without stone With stone
(b) Active	Without stone With stone
IV. Miscellaneous	Without stone With stone

Group I represents microscopically normal gallbladders and those in which but minimal signs of inflammatory changes are apparent, while Group II consists of those in which somewhat more obvious microscopic evidences of cholecystitis are present with but little or no associated fibrosis. The pathological changes reported in either category are considered to be insufficient to account for loss of concentrating power. Although Graham believes that gallbladder dysfunction is not necessarily attended by demonstrable or apparently comparable microscopic changes, this means of measuring diagnostic accuracy is more easily defended before roentgenologists than a yardstick which depends upon the patient's statement of disappearance of symptoms following cholecystectomy. If erroneous conclusions regarding dependability result from such methods of proof, the effect must be to render accuracy of figures as presented by the roentgenologist more conservative rather than otherwise.

Under Group III, major inflammatory disease, moderate to severe chronic cholecystitis, chronic cholecystitis with definite fibrosis, as well as active, subacute, purulent, ulcerative cholecystitis, etc., are included. Any of these conditions may readily be recognized in the gross or microscopic findings beyond question of dispute. The miscellaneous conditions listed under Group IV include neoplasms of the gallbladder or ducts and a single unusual case of periarteritis nodosa.

A preliminary sorting of all data according to roentgen diagnosis showed the relative frequency of various roentgenological observations as well as the total number of cases later subjected to proof in each group (Table II). Discarding all unverified cases, the remaining 238 were re-sorted to determine to what degree roentgen findings were in agreement with direct surgical or pathological observations. At this point it became apparent that it would be highly desirable, if not indeed imperative, to investigate the validity of roentgen observations regarding the concentrating power of the gallbladder and the presence or absence of stone separately. Whether or not the existence of biliary calculi affect concentrating power, it is obvious that the roentgenologist's opinion is built upon two entirely different types of evidence in the recognition of cholelithiasis and in determining the status of gallbladder function.

Cholelithiasis. Before the advent of cholecystography the part played by roentgenology in the diagnosis of biliary disease rested primarily upon the direct visualization of calculi. Although in this particular study no attempt was made to include cases in which stones were recognized by the roentgen ray during examinations other than cholecystography, it is interesting to note the number of instances in which calculi were correctly identified even when no gallbladder shadow was obtained. Figure 1 diagrammatically represents the roentgen findings in those proved 88 instances of cholelithiasis without visible dye shadow in cholecystographic films. Only 32 per cent of the stones in these cases were recognizable roentgenographically. Considering the entire group of cases in which biliary calculi were proved to be present at operation, stones were recognized by cholecystog-

raphy in 49 per cent. The improvement in reliability is easily explained by the fact that stones insufficiently dense to cast shadows themselves were seen as defects in shadows cast by slightly or greatly con-

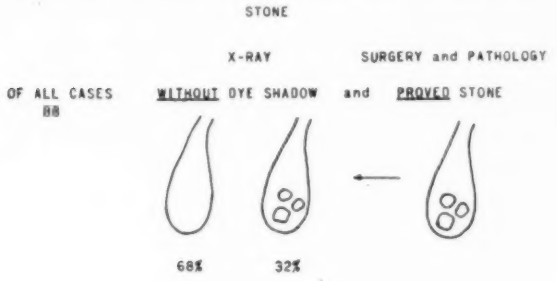

Fig. 1

centrated dye. It is noteworthy that normal visualization without stones was never reported in the case of patients later shown to harbor calculi. The inescapable coincidence of stone transparency and absence of dye shadow occurred with sufficient frequency to prevent a closer approximation to perfect prediction of operative findings (Fig. 2). If one considers only those proved stone cases in which previous dye feeding resulted in sufficient concentration within the gallbladder to render this organ visible, this annoying group in which stone recognition is impossible is ignored and accuracy of prediction approaches perfection, 94 per

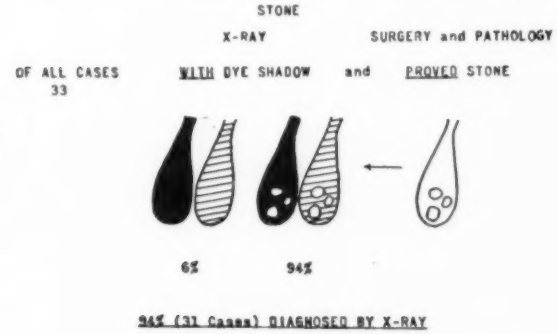

Fig. 3

cent (Fig. 3). One may therefore conclude that cholecystographic examination greatly assists in recognizing stones when they exist, that in those cases where dye shadows are present diagnostic accuracy is of

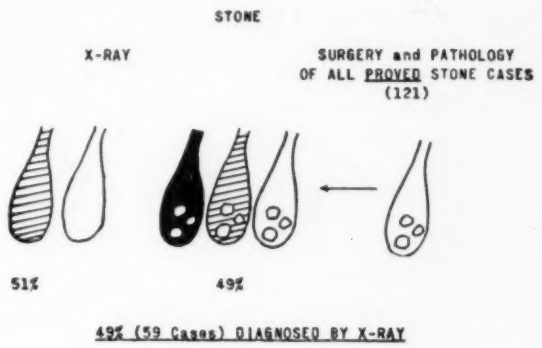

Fig. 2

an exceedingly high order (Table IV).

To reverse one's approach to the matter of stone recognition it remains to inquire as to the correctness of all roentgen reports describing stones in the entire group of 238 cholecystographic examinations later sub-

Table IV

SUMMARY

Cases with Proved Stones

No. Cases		Roentgen Diagnosis of Stone	
88	No dye shadow	28	32%
121	All cases	59	49%
33	Dye shadow	31	94%

jected to surgical or pathological inquiry. Normal visualization with stone and faint visualization with stone combined were reported 33 times with but one proved error. Non-visualization with stone, reported 32 times, was disproved as regards stone again in but one instance (Fig. 4).

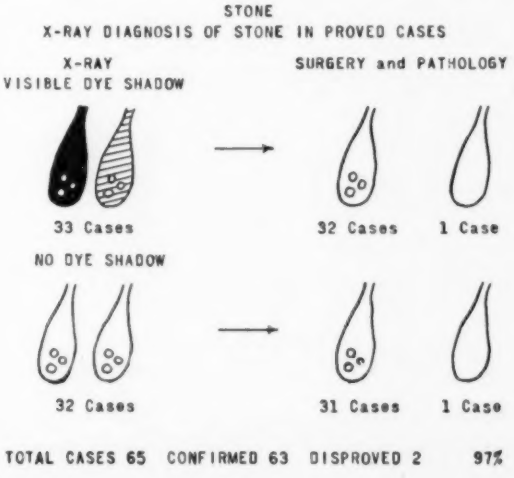

Fig. 4

From these observations one may conclude that although roentgen studies may justifiably fail to reveal biliary stones whenever present, even though the procedure of cholecystography is employed, when by this method stones are reported subsequent confirmation may be expected 97 times in 100.

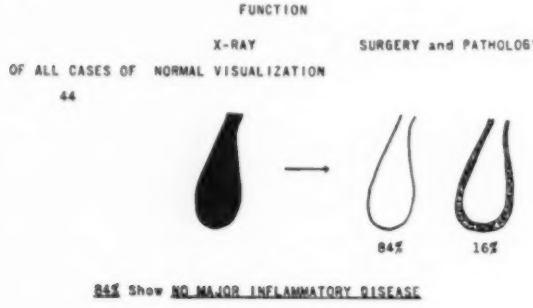

FIG. 5

Cholecystitis. The discovery and description of biliary calculi is one matter; the expression of an opinion regarding the probability of existing disease of the gallbladder wall is quite another. Granted that cholecystography merely aims to determine the concentrating ability of the gallbladder, this test is admittedly employed widely in medical practice to confirm or disprove a provisional clinical diagnosis of cholecystitis. Unfortunately it is even requested at times together with numerous other roentgen and laboratory tests on the chance that entirely unsuspected disease of the gallbladder may be disclosed. On occasion one finds that he has been asked to conduct the examination at the express request of the patient whose physician acquiesces to the demand with little thought that any information of value will be forthcoming. Viewed in this light, the probable significance of the particular situation one may report concerning the gallbladder's ability to concentrate bile becomes worthy of careful consideration.

If one selects from the case material upon which this investigation is based the 44 cases reported by roentgen examination to show "normal gallbladder visualization" and inquires into the subsequent pathological findings as reported according to the described classification, one finds that not all of these gallbladders were innocent of disease. Despite the fact that concentrating power had been maintained, 16 per cent were definitely diseased (Fig. 5). However, one might have reported "normal gallbladder," omitting any reference to function and referring directly to the presence or absence of inflammatory disease, with 84 per cent accuracy.

When the gallbladder shadow, though visible, is exceedingly faint, the personal factor in judging the degree of density becomes apparent, for in but 61 per cent of the 23 cases so reported was major gallbladder disease subsequently proved to exist (Fig. 6).

Of the 238 cases subjected to proof as to gallbladder status after cholecystographic examination, 21 were shown to be involved with major inflammatory disease and to be free of stones. Reviewing the roentgen findings reported in these instances, one finds that impaired function was described in 95 per cent. In other words, only 5 per

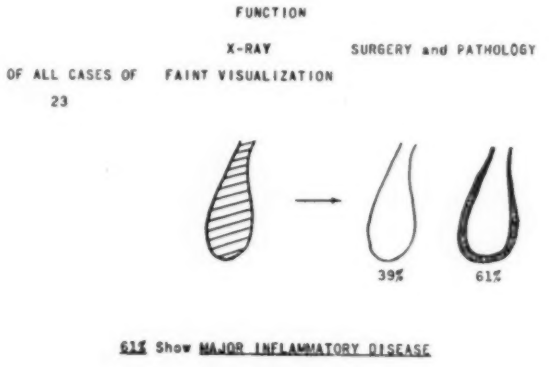

FIG. 6

cent of these patients had been given false assurance regarding the status of their gallbladders (Fig. 7).

A larger group of patients were found at operation to be affected with major inflammatory disease complicated by the presence of stones. Referring to the previous roentgenologic opinions ventured, one again finds that the inflammatory changes were recognized by virtue of impaired con-

centrating power in 94 per cent (Fig. 8).

The presence of biliary calculi appears to exert a definite influence upon the concentrating power of the gallbladder, for of 121 cases with proved stone but 15 showed normal visualization, and yet this cannot be a direct effect since roentgen evidence of impaired function is observed in virtually the same proportion of cases with proved inflammatory disease regardless of whether stones were present or absent. Roentgen findings were indicative of some type of abnormality, either cholelithiasis or depressed concentrating power of the gallbladder, in the case of every patient in whom calculi were later found (Table v).

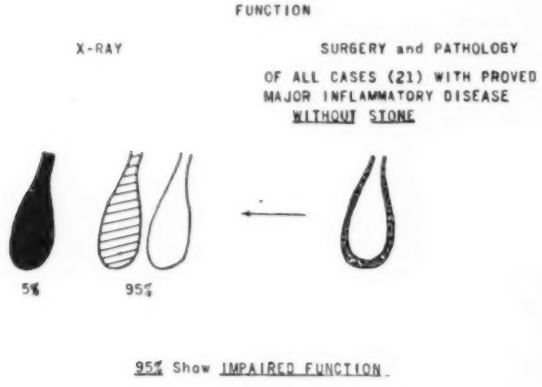

Fig. 7

Table V

ROENTGEN DIAGNOSES IN CASES WITH PROVED STONE (121)

15 cases	Stone (normal visualization)
18 cases	Faint visualization with or without stone
88 cases	Non-visualization with or without stone

It follows that if the roentgenologist could choose in advance the case material best suited to display his ability to make correct diagnoses from cholecystographic data, he would do well to accept for examination only those patients strongly suspected of harboring biliary calculi.

The most severe test of the accuracy of predicting inflammatory disease of the gallbladder is made when all cases of reported non-visualization are examined in the light of subsequent findings. Under these circumstances one must reckon with technical errors, all of which may be expected to interfere with visualization.

Of 131 patients reported to show complete invisibility of the gallbladder after the dye, 20 per cent were subsequently shown to be normal or but slightly inflamed (Fig. 9). In the case of the remaining 80 per cent, however, non-visualization was amply explained on the basis of major inflammatory changes.

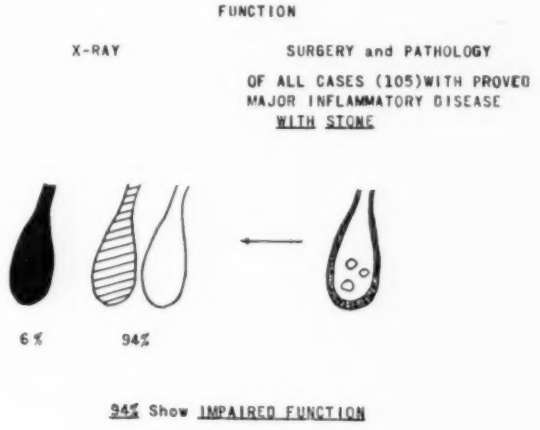

Fig. 8

To the very practical question of the internist or surgeon who wishes to know, "Is this patient's gallbladder diseased? Does she have cholecystitis?", it appears that based upon the experience of this department one may confidently answer in the affirmative if the gallbladder fails to visualize, expecting later corroboration in 80 per cent of such cases. Al-

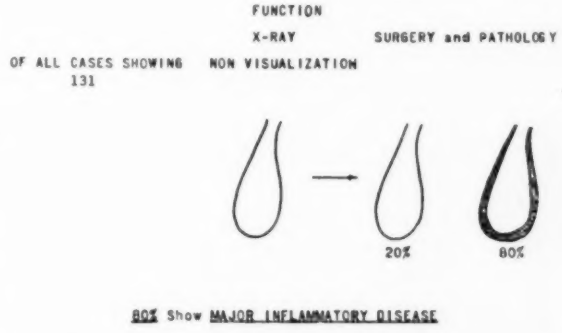

Fig. 9

though we must expect a 16 per cent error, if we interpret normal visualization as insurance against major inflammatory disease and a 20 per cent error if we assure our clinical staff that patients whose gallbladders do not visualize will be found to have cholecystitis, we are on exceedingly certain ground when we tell them that if a given patient actually suffers from major cholecystic inflammation, as he suspects, that patient's gallbladder will not properly concentrate bile, for over a two year period only 7 errors of that sort have been reported in a group of 126 patients.

CONCLUSIONS

Cholecystographic examination, designed to gauge gallbladder function, serves two practical diagnostic purposes: (1) to materially improve accuracy in the matter of the recognition of existing biliary stones and (2) to prognosticate with reasonable certainty existing inflammatory disease of the gallbladder.

Recognition of calculi is 97 per cent reliable in those cases where sufficient concentrating power is retained to permit visualization of the gallbladder in any degree.

Impaired concentrating power of the gallbladder is frequently associated with cholelithiasis; in this series the coincidence is 87.6 per cent. The extent of this coincidence may well reflect accepted indications for surgery of the gallbladder.

Cholelithiasis is always attended by some deviation from normal cholecystographic findings.

Normal response to the cholecystographic test of gallbladder function may be considered 84 per cent accurate in excluding major inflammatory disease.

Complete non-visualization of the gallbladder is associated with major inflammatory involvement of the gallbladder wall in 80 per cent of all cases so reported.

We are greatly indebted to Dr. Carl V. Weller for counsel and assistance in evaluating microscopic evidence of gallbladder disease in this series of cases. We are also indebted to Dr. Bernard D. Harrington for valuable assistance in the tabulation of case material.

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DISCUSSION

Dr. I. S. RAVDIN, Philadelphia. I am greatly impressed with the thoroughness with which this study has been carried out. It is the type of statistical compilation which adds to our knowledge of the subject and which is therefore of real value. It is because of the thoroughness with which the data have been collected that a discussor finds difficulty in doing more than making a few complimentary remarks.

There are a few aspects of the problem, however, which may be open for further discussion. I believe that wherever possible the first film should be of such size as to include the entire abdomen. The varied position of the gallbladder, as seen at operation, would seem to justify a wide exposure for the first film.

I was surprised that in the very large series reported in the paper not a single instance of a gallbladder containing "milk calcium" was observed. Unless a film is made of the gallbladder area prior to the administration of the dye this condition may be overlooked and the gallbladder reported as a normally concentrating viscus. Even though the preliminary film is not made it is possible to diagnose the condition with considerable accuracy by the failure of the gallbladder to empty at least a portion of its contents after the fat meal.

It is now time that this Society initiate a standard nomenclature for reporting the results of cholecystographic study. Whether the nomenclature suggested by Kirklin and used

in the authors' paper is the most satisfactory one for universal application should be carefully considered. Since cholecystography gives information not only of the concentrating function of the gallbladder but also on the ability of the gallbladder to evacuate its contents some classification which includes the terms functioning and abnormally functioning would seem appropriate.

In one particular I must take exception to the reasoning which Drs. Hodges and Lampe have adopted. Our studies on the chemical composition of the gallbladder bile removed at operation have given us the opportunity of comparing the pathological report with the chemical findings. We must agree with Graham that evidence of minor histologic changes in the gallbladder wall is of little help in determining whether or not cholecystitis, of a degree capable of producing symptoms, exists. The end-results of cholecystectomy in the absence of gallstones are so bad that surgeons now realize that regardless of the cholecystographic evidence, and regardless of a pathologist's report, it is very likely that in well over half of the operated cases the gallbladder does not account for the patient's symptoms. The 16 per cent error which the authors found when they interpreted normal visualization "as insurance against major inflammatory disease" is to be expected since it not infrequently occurs that a gallbladder which has been the site of a major inflammatory process recovers sufficiently to give normal visualization.

At a time when clinicians lean more and more on certain laboratory examination as an aid to more accurate diagnosis, it is comforting to know that properly controlled cholecystography occupies a place in diagnosis of which the roentgenologist can justly feel proud, and upon which the clinician can place great reliance. Although the number of verified cases in the present series is small, the care with which the data have been prepared and the caution which the authors have exercised in their deductions make this report doubly valuable.

Dr. Hodges (closing). We are grateful for Dr. Ravdin's kind remarks and his consideration of the paper we have submitted. In answer to his query regarding the routine search for calcium bile, it may be said that prior gastrointestinal examination afforded this opportunity in the majority of our cases. Our experience in this matter is exceedingly limited, however. We quite agree with what he has to say about terminology and hope that the present lack of uniformity may one day be overcome. We also agree that pathological findings at the microscope are not the last word in determining the cause of faulty visualization. We chose microscopic evidence of inflammation as the most definite and concrete criterion at present available.

POSTOPERATIVE VISUALIZATION OF THE BILIARY TRACT

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THE desire to further dispel the element of doubt from the mind of the surgeon as to the proper time to remove the common duct drainage tube after choledochostomy prompted us to take up this study. Any method which makes less likely a premature removal of common duct drainage tubes should receive careful consideration by all who deal with these cases.

The procedure described by Overholt[9] in his experiences in 11 such cases called our attention to the possibilities of roentgen visualization of the biliary tract by means of an opaque medium. Since that time, January, 1931, on the service of Dr. Fred M. Douglass, we have employed this method in the examination of 45 cases of common duct drainage.

Its value has been demonstrated in some measure in every one of these cases, and, in a few instances, it has proved to be a remarkable aid in the postoperative care of these patients.

HISTORY

The way to the use of radiopaque substances for the investigation of common duct drainage cases was first pointed out by the observations of Piccinino and Pazienza[10] in the injection of biliary fistulae with an opaque medium.

Mallet-Guy, Beaupère and Armanet[8] used lipiodol in biliary fistulae and report a severe reaction following its repeated injection in one case. They attribute this reaction not to shock or to iodism but rather to a pancreatic edema. Their explanation of the cause of this is not exactly clear.

Later, in 1928, Caeiro[1] reported his experiences with the investigation of biliary fistulae by lipiodol.

In 1929 Cotte[2] reported a series of cases in which he had injected lipiodol into the common duct drainage tube. He twice, in a series of 20 cases which had been operated on for lithiasis, demonstrated by roentgenography calculi that had escaped notice in the first operation. He further observed that certain parietal lesions, such as cicatricial constriction of the choledochus, may be demonstrated.

Ginzburg and Benjamin,[6] in 1930, added a valuable suggestion in their reported lipiodol studies of postoperative biliary fistulae. They stated that these injections were best made under roentgenoscopic control, thus visually determining the patency of the common duct.

The first to see the advantages of investigation of the biliary tract by opaque media injected through a T-tube in the common duct was Gabriel.[5]

In the series of cases which Overholt[9] reported in 1931 many valuable observations were made regarding the filling of the hepatic ducts when the common duct was obstructed. A close correspondence was noted between the degree of dilatation of the hepatic ducts and "the degree of liver drainage as estimated by the biliary output, the change in Van-den-Bergh reaction, and the duration of the convalescence."

The T-tube method of draining the biliary tract after common duct operations has received its most ardent support from Judd. Its widespread use now attests its value where prolonged drainage is necessary after common duct operations. Judd and Phillips,[7] in reporting a series of 40 cases in which an opaque medium was injected through the T-tube and roentgenographic studies made, stated their belief that "this method of determining the patency of the common duct affords a better understanding of post operative conditions in the biliary tract which have necessitated drainage by the T tube."

RADIOPAQUE MEDIUM USED

In the choice of a radiopaque medium which is to be injected into any part of the body certain definite factors should be considered. Viscosity, stability under heat or in contact with body tissues, qualities of visualization, and cost are all important factors.

In the early work in biliary tract visualization lipiodol was used and later discarded for campiodol. The work of Frazier[4] popularized the use of campiodol or rapeseed oil for all types of roentgenographic exploration because of its low specific gravity, low viscosity, stability and good tolerance by all body tissues.

The investigations on halogenated oils employed in roentgenography by Tabern and his collaborators[11] have shown fairly conclusively that the brominized vegetable oils are preferable in most instances when stability is an important factor.

Because of these facts and the lower cost of brominol, we early gave up the use of campiodol in this work. The average amount of brominol used is 20 c.c.

TECHNIQUE

The average common duct drainage case is sent to the roentgen department for a brominol injection on the twelfth to the twentieth postoperative day.

The patient is placed on the roentgenoscopic table and an ordinary urethral irrigating syringe with a compressible rubber bulb is connected to the T-tube. The clamp is then removed from the tube and the syringe is lowered to the patient's side to allow as much of the biliary fluids to drain off as possible. Gentle suction may be used to start the flow. The syringe is then elevated and the bulb removed, allowing the level of fluid in the tube to reach the tip of the syringe, so that no air may be present in the drainage tube.

The brominol which has been warmed to body temperature is then poured into the syringe and the bulb is replaced. Care is taken that the syringe is not elevated to the point of starting the flow of brominol into the tube until the operator is prepared to switch off the lights, remove his dark glasses and start roentgenoscopy.

The syringe is then elevated usually to a height of 8 to 12 inches to start the flow of brominol. Often some pressure is applied to the rubber bulb to induce sufficient flow. The injection is made very gently and slowly and the patient is instructed to inform the operator of the first indication of pain or distress.

From time to time the roentgenoscopist replaces his dark glasses and the lights are switched on to determine accurately the remaining amount of brominol in the barrel of the syringe. The unexpected injection of air into the tube is thus obviated. The entire injection is ordinarily made in less than five minutes.

If the common duct is freely patent the opaque medium will be seen to pass readily into the duodenum and may only partially outline the duct, with little, if any, medium getting into the intrahepatic ducts. If some degree of obstruction is present, fairly rapid filling of the common duct may be effected with almost immediate filling of the hepatic radicles and the intrahepatic ducts. Care is taken not to overdistend the biliary ducts, though there is little danger of this if the injection is stopped on the first expression of discomfort by the patient.

At the close of the injection the tube is reclamped and the syringe is removed.

A roentgenogram is taken at once if opaque medium has been observed to pass into the small bowel. If not, fifteen minutes is allowed to elapse and the roentgenogram is then made. This film is processed and examined. If no opaque medium is evident in the small bowel another roentgenogram is made thirty minutes later and this is examined. If no opaque medium is seen in the small bowel at this time the duct is considered not to be patent and re-examination at a later date is advised. However, only a degree of patency which will allow the medium to pass into the bowel in the first fifteen minutes is usually considered safe for removal of the drainage tube.

In most cases the primary interest of both the roentgenologist and the surgeon is the degree of patency of the common duct. There are, however, many other valuable observations to be made in these examinations, both roentgenoscopically and from the roentgenogram. The extent of the information which can be obtained from these studies is limited only by the number of cases examined. Each case presents some new phase or new aspect of the problem of postoperative care of common duct surgery.

In studying the roentgenograms made after the injection of the opaque medium, the following points should be observed: (1) the type of drainage tube, its direction and point of entrance into the common duct; (2) the size and shape and extent of filling of the common duct, with possible filling defects from stones or strictures; (3) the presence or absence of a cystic duct; (4) the extent of filling of the hepatic ducts and the intrahepatic ducts, their appearance as to dilatation, blunting or clubbing, and possible filling of the smaller ducts forming arborization patterns; and finally (5) the presence or absence of opaque medium in the small bowel, its amount and distribution.

The observation of these structures and their appearance both under the roentgenoscope and in the roentgenogram will add materially to the information which the surgeon has obtained clinically, and aid him in choosing the proper course in the follow-up care of these patients.

FIG. 1. Case 1. *T*, tube in common duct; *CD*, common duct, not dilated; *H*, hepatic ducts, extensively filled, little dilatation; small intra-hepatic ducts, well filled; arborization; *B*, opaque medium free in the small bowel; common duct freely patent.

CASE REPORTS

The following cases are chosen from a series of 45 in which injections of opaque medium were made after some form of gallbladder and common duct surgery. They serve to illustrate most of the conditions found in biliary tract surgery, as well as some of the errors occasionally made in this type of work.

CASE 1. Mrs. J. H., aged sixty-two. Patient

entered St. Vincent's Hospital on July 8, 1931, with the complaint of pain in the right upper abdomen, associated with eructation of gas and "sour fluid." The history revealed the occurrence of similar attacks for the past two years with increasing frequency and severity. Attacks were always characterized by severe pain usually radiating to the right shoulder. Nausea and some vomiting, occasional mildly acholic stools, slight icterus, some weakness and some loss of weight had occurred.

roentgenogram shows a fairly well-outlined common duct, appearing slightly dilated. The intrahepatic ducts, both right and left, are extensively filled to the point of marked arborization; a fairly large amount of opaque medium is present in the small bowel, indicating patency of the common duct.

Because of pain experienced by the patient at end of injection, followed by some nausea and vomiting and slight rise of temperature, a subsequent film of the liver area was made

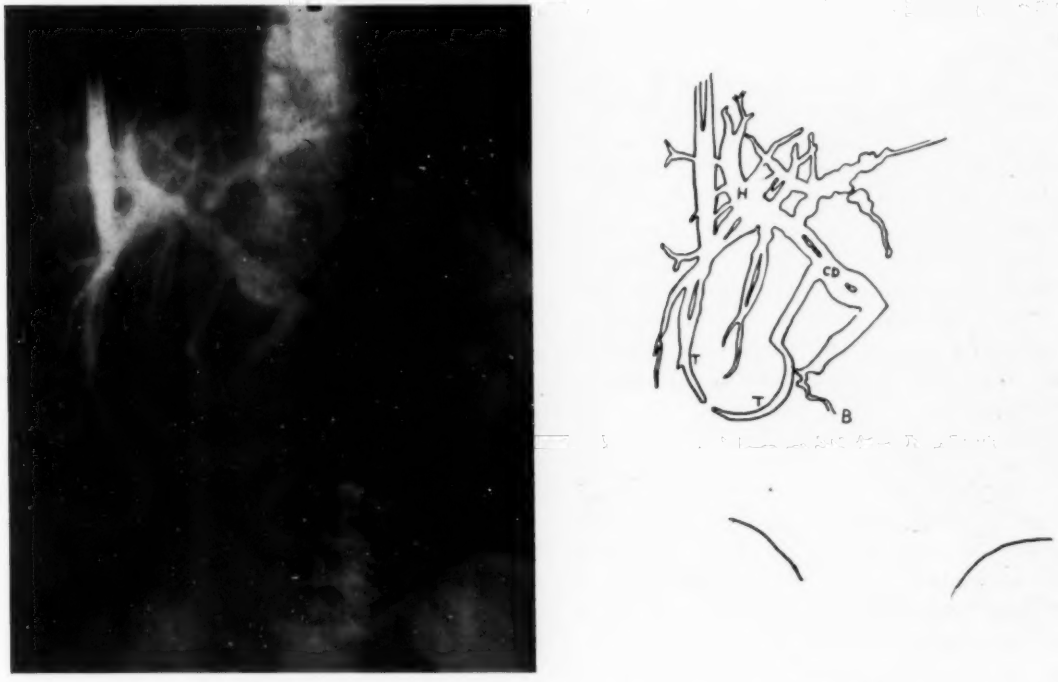

Fig. 2. Case 11. *H*, hepatic ducts dilated, some blunting; *CD*, common duct dilated; *B*, some opaque medium present in duodenum. Common duct patent.

At operation the gallbladder was small, adherent to the duodenum, and contained stones. The common duct was dilated and there were many glands along its course. The head of the pancreas was enlarged. Cholecystectomy. Choledochostomy. The common duct was probed and found free from stones or stricture. T-tube sutured in place. Routine appendectomy. Normal convalescence except for some postoperative nausea. The bile flow was small, 100 c.c. for the first twenty-four hours.

Three weeks after operation 20 c.c. of campiodol was injected slowly through the T-tube, not under roentgenoscopic control. Near completion patient complained of some fullness in upper abdomen and slight pain. Immediate twenty-four hours later. A very small amount of opaque medium was still evident in the hepatic radicles. No further trouble was experienced by the patient and the tube was removed two days later. One year later patient returned to the surgeon for examination, symptom-free and gaining in weight.

Comment. As well as serving to illustrate what one should not do in these cases, viz., inject a common duct drainage case without roentgenoscopic control, this case offers evidence of remarkably little hepatic duct involvement though the history of cholecystitis is of at least two years' duration. The fact that no obstruction was found in the

common duct at operation and patency was demonstrated in the roentgenogram three weeks postoperatively, and the intrahepatic ducts showed little, if any, dilatation with no blunting or clubbing, would seem to indicate that in spite of the fairly long-standing infection stasis in the biliary tract was not a prominent feature.

That a good prognosis might be expected in this case from the appearance of the relatively normal biliary tract was substantiated by the splendid recovery of the patient.

CASE II. Mrs. E. R., aged thirty-eight. Patient entered St. Vincent's Hospital on November 5, 1931, with the complaint of pain in the abdomen recurring frequently during the previous five or six weeks. Prior to that time patient was always well, except for an occasional "backache." These attacks were characterized by pain confined mostly to the right upper abdomen with some radiation to the back. Some complaint of nausea without vomiting. Constipation moderate. Slight jaundice. Icterus index 10 per cent.

A large distended gallbladder with stones was found at operation. The common duct was opened and contained four stones. The patency of the common duct was established by probing and a T-tube sutured into the duct. The gallbladder was removed. Appendectomy routine.

Cultures from the gallbladder and bile showed no growth.

The pathologist reported a chronic active infection of the gallbladder.

Three days after the operation the patient developed a bronchopneumonia. Convalescence delayed. The bile drainage averaged 300 c.c. daily.

Twenty-eight days postoperatively 20 c.c. of brominol was injected through the drainage tube under roentgenoscopic control. The common duct and the liver ducts were readily filled with only a small amount of opaque medium seen to pass into the duodenum.

Films were made immediately after injection. The common duct is markedly dilated. The intrahepatic ducts are well outlined, with some portions showing clubbing and other portions with some degree of arborization present. There is a very small amount of opaque medium evident in the small bowel.

Examination repeated five days later with similar findings except for less evidence of arborization present and more opaque medium evident in the small bowel. These films were made fifteen minutes after injection. T-tube removed eight days later. Patient remained well.

Comment. Though the history of gallbladder trouble in this case is relatively of short duration, five to six weeks, the evidence found at operation would indicate a long standing infection. The gallbladder wall was chronically inflamed. Stones were present in the gallbladder and in the common duct with marked dilatation of the duct. The findings in the biliary tract visualization would tend to indicate the presence of long-standing infection. Note the large dilated common duct and the dilatation of most of the hepatic ducts. The filling of some of the smaller hepatic ducts in the first film may be explained on the assumption that the bile in these radicles was less viscous at this time. Good drainage of 300 c.c. daily average had been continued twenty-eight days. However, the possibility of a less advanced involvement of the intrahepatic ducts of these lobules of the liver must be considered.

An error of technique was made in this case in not taking a roentgenogram at least fifteen minutes subsequent to the injection on the first occasion. This would perhaps have obviated the necessity of a second examination, five days later, when opaque medium was found in the small bowel indicating patency of the common duct. Proof of the ampleness of this patency was the fact that eight days later the drainage tube was removed and the patient remained well.

CASE III. W. M. H., male, aged forty-seven. Patient was admitted to St. Vincent's Hospital on September 10, 1933, at the close of a severe attack of pain in the right upper abdomen, which radiated to the right shoulder. Several attacks of this nature had been experienced during the preceding two years. Jaundice was a prominent feature in most of them. Clay-colored stools accompanied each attack. No chills or fever had been noted, though patient entered hospital with a temperature of 99°F., pulse 80.

After two days of preparation patient was

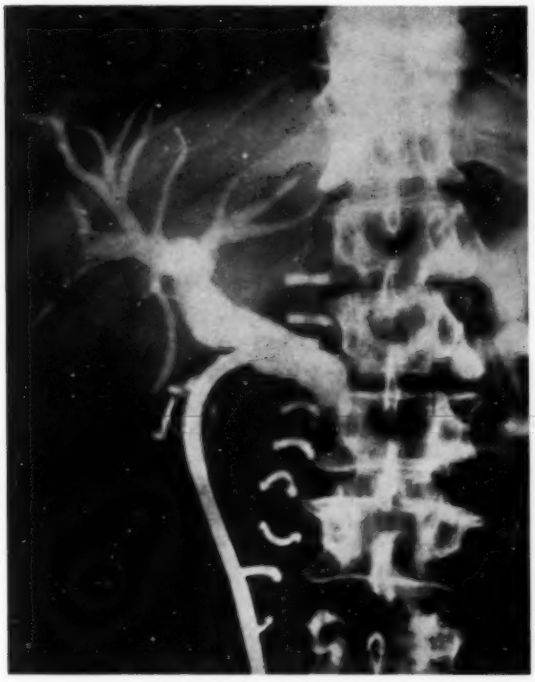

Fig. 3. Case III. *T*, tube in common duct; *CD*, common duct markedly dilated; *H*, hepatic ducts dilated, some blunting; no opaque medium in small bowel.

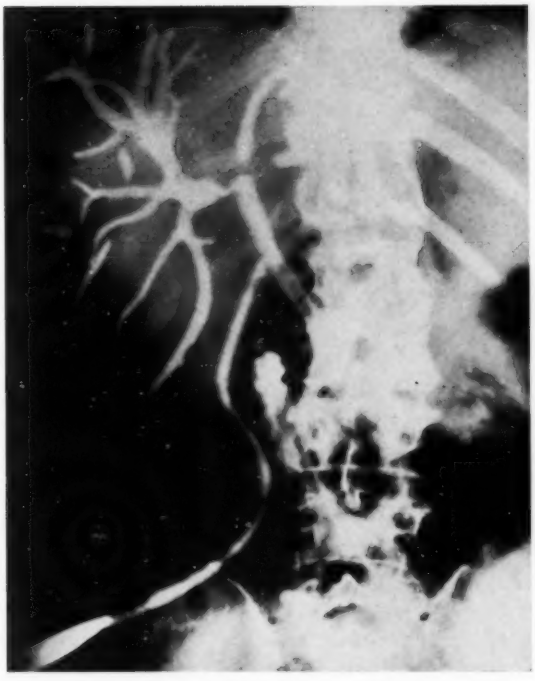

Fig. 4. Case III. *T*, tube in fenestrated indwelling catheter; *H*, hepatic ducts still dilated and clubbed; *B*, some opaque medium in the bowel; *IC*, indwelling catheter in common duct.

operated upon—cholecystectomy and choledochostomy. The gallbladder was contracted and small, containing several stones. The common duct was greatly dilated and contained gravel but no large stones. T-drainage tube was placed in the duct. Convalescence was uneventful. Bile drainage was 300 to 400 c.c. every twenty-four hours. Culture from the gallbladder revealed staphylococci.

On the twelfth day after the operation, brominol was injected under roentgenoscopic control through the T-tube. The common duct was visualized and appeared greatly dilated. The intrahepatic ducts were dilated and blunted. No opaque medium was observed to pass into the small bowel. A roentgenogram made fifteen minutes later substantiated these findings. The T-tube was clamped for one and one-half hours and then released. A film made immediately after release of the tube shows some opaque medium still remaining in the liver radicles and the common duct. None is evident in the small bowel. Patency of duct not established.

A recheck examination was made eight days later. Findings practically the same with T-tube in place. No opaque medium was evident in the small bowel.

The tube was then clamped for two days without discomfort to the patient. Patient sent home. Twelve days later patient returned for observation stating the tube had been clamped for nine days without any pain. The tube was then removed, thirty-one days postoperatively.

Three weeks later patient reported at office with no complaints, feeling fine and a gain of 16 pounds in weight. The wound was healed.

Three months later, on February 2, 1934, the patient returned with slight jaundice, slight pain, no weight loss and normal stools.

An inflammatory obstruction or possibly overlooked stone was considered and the referring physician was advised to send patient back for observation in one week. Patient did not return until September, 1934, seven months later. There was now definite pain and recurring attacks of jaundice.

On October 30, 1934, patient again entered the hospital and at operation a large liver was found. The common duct was dilated and some small gravel was found in the ampulla of Vater. Difficulty was experienced in passing a probe through the common duct into the duodenum. A catheter was then placed in the duct and allowed to project into the duodenum with the funnel end anchored just below the junction of the right and left hepatic ducts, after the method of McArthur. A T-tube was placed through an eye in the catheter for external drainage.

Normal convalescence followed with the patient returning to the office about every three weeks for observation. A steady gain in weight has continued and patient has been free from symptoms. Stools normal in color.

On February 12, 1935, brominol injected through T-tube under roentgenoscopic control with the following findings: The common duct well visualized and appears dilated. The in-lying catheter is seen extending into the duodenum. Roentgenogram thirty minutes subsequent to injection shows a small amount of opaque medium to have passed into the small bowel. The intrahepatic ducts show dilatation and marked blunting.

March 19, 1935, re-examination: Brominol injection through the common duct drainage tube shows the in-lying catheter in the common duct and duodenum in the same position as on previous examination. The hepatic ducts are outlined throughout and appear blunted. The common duct is well outlined and markedly dilated. Roentgenogram thirty minutes later shows a fairly large amount of opaque medium in the upper small bowel. The liver ducts remain well filled. Patency of the common duct not definitely established.

Comment. This case demonstrates the danger of removal of a common duct drainage tube until a visual confirmation of its patency is obtained. Mere absence of pain following even prolonged clamping of the tube is not sufficient to guarantee an adequate patency of the common duct.

The recent findings after brominol injection show fairly definitely that even though drainage is carried on over long periods (in this case over four and one-half months), the biliary tract system may continue to show the evidences of a long-standing infection. This is indicated by the persistence of the dilated common duct and the dilated and blunted intrahepatic ducts.

From a technical standpoint this case illustrates an excellent method of insuring good drainage of the biliary system by a combination of McArthur's indwelling catheter and a T-tube placed in the fenestrated catheter. By this means Dr. Fred

M. Douglass has on several occasions made possible continued drainge of the reconstructed common duct until such time as the in-lying catheter frees itself and passes down the bowel.

Case iv. Mrs. A. S., aged thirty. Patient was admitted to St. Vincent's Hospital on June 13, 1932, complaining of pain in the right upper abdomen. For eleven years she had had symptoms referable to the gallbladder. Her attacks had sometimes been associated with jaundice though none was evident at this time. Icterus index 10. Wassermann reaction negative. Temperature 99.4°F., pulse 90.

The patient was prepared for operation, which was performed one day later. Cholecystectomy and appendectomy. Gallbladder was filled with stones. The common duct was found negative to palpation. Duct not dilated. Culture from gallbladder walls showed no growth. Patient was discharged on the fourteenth day after the operation with no complaints.

Eight months later, on February 9, 1933, patient returned to the hospital with severe pains similar in character to those experienced previous to the cholecystectomy except that at this time the distribution appeared more widespread and extended into the epigastrium. There was no jaundice at this time. Icterus index 8.3. The patient was prepared and two days later at operation the common duct was isolated and opened. Duct not appreciably dilated at this time. On opening it was found to contain four facetted stones, one taken from the ampulla of Vater. A probe was passed into the duodenum and hepatic ducts. Patency of common duct established. Choledochostomy was completed and a T-tube was sutured into the duct for drainage. Convalescence uneventful. The bile drainage was satisfactory and sixteen days postoperatively 12 c.c. of brominol was injected through the T-tube into the common duct under roentgenoscopic control. There was a ready passage of the opaque medium into the duodenum. The roentgenogram made subsequently shows a very small amount of the opaque medium present in the hepatic radicles, without marked dilatation evident. The common duct does not appear to be markedly dilated. A large amount of the opaque medium is seen distributed through the upper small bowel. Patient returned for observation in August, 1934, free from symptoms and in good health.

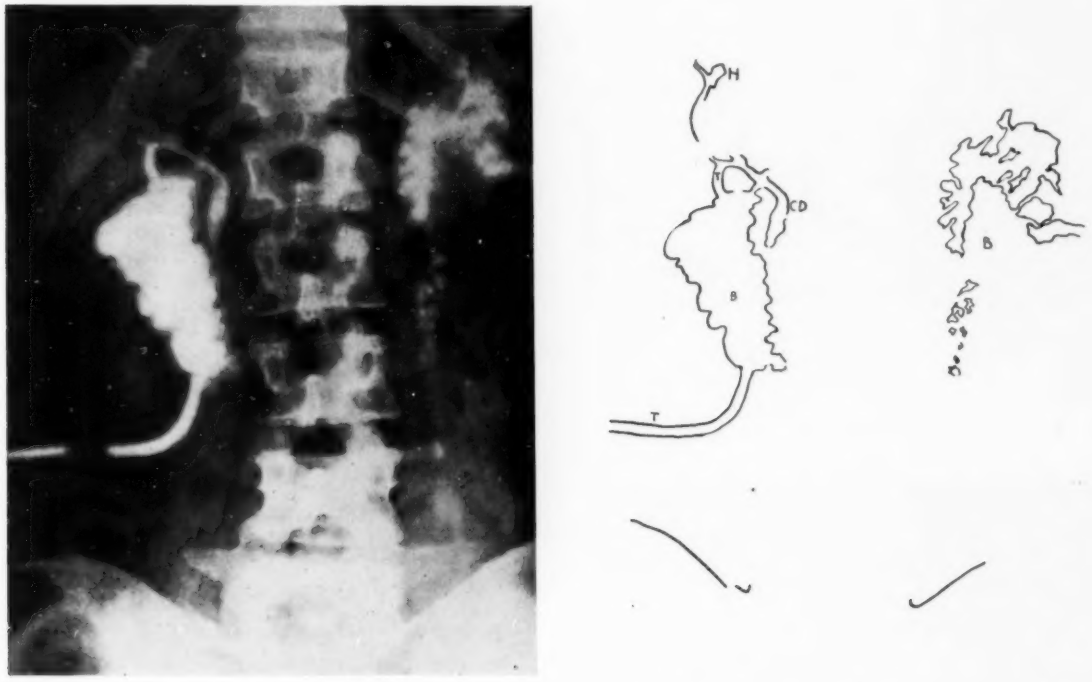

Fig. 5. Case iv. *T*, tube in common duct; *B*, large amount of opaque medium distributed in small bowel; *CD*, common duct not dilated, freely patent; *H*, poorly filled hepatic ducts, no evidence of dilatation. Brominol injection 12 c.c.

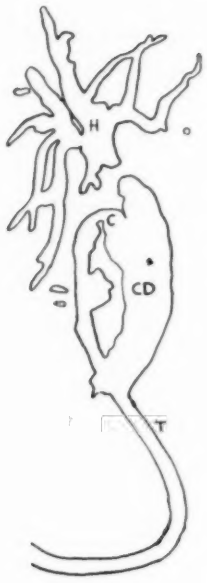

FIG. 6. Case v. *T*, tube in stump of cystic duct; *CD*, common duct markedly dilated; *H*, hepatic ducts dilated; marked clubbing and blunting. No opaque medium in small bowel.

FIG. 7. Case v. *T*, T-tube one short limb in common duct; *CD*, common duct dilated; *H*, hepatic ducts still blunted and dilated; no opaque medium in the small bowel.

Comment. This case is remarkable in that though there was a prolonged history of eleven years' duration of symptoms referable to the gallbladder, no evidence of dilatation of the common duct was demonstrated at either the first or the second operation. The presence of facetted stones in the common duct eight months after the first operation leads one to question their absence on that occasion. The difficulty of palpation of small stones in the common duct is a well-recognized fact. A tube inserted into the common duct at this time with a subsequent opaque medium visualization might possibly have revealed their presence. Earlier removal might then have been possible with a consequent saving of time, pain and anxiety to the patient.

Case v. Mrs. M. A., aged twenty. Patient entered St. Vincent's Hospital on July 31, 1934, with complaint of aching and sometimes sharp pain in the right upper abdomen and under the inferior angle of the right scapula.

Four months previously patient had been in the hospital for a week with a symptom-complex suggestive of marked hepatitis and cholecystitis. A diagnosis of probable amebiasis was made. Patient rapidly improved on anti-amebic therapy, though no amebic cysts were ever found in the feces.

Seven months previously patient had had a very severe attack of "indigestion" associated with "heart burn," nausea, belching and acid eructation. These symptoms were followed by pain which had no relation to the type of food eaten nor were they relieved by diet. She had had a pelvic operation two years before, salpingectomy and appendectomy. For seven years past the patient had symptoms referable to the gallbladder. With all recent attacks slight jaundice was present. No chills. The icterus index was 14.2 in July, 1934; the red blood count was 4,200,000, the white blood count 11,000. Wassermann reaction negative.

The patient was prepared for operation and two days later, on August 1, 1934, a cholecystectomy and choledochostomy were done. The gallbladder showed a subacute cholecystitis with stones present. The common duct was dilated and inflammatory glands were present along the duct. No stones were found in the common duct.

A catheter was placed through the stump of the cystic duct into the common duct for drainage. Convalescence was uneventful. The drainage was from 150 to 250 c.c. every twenty-four hours. The jaundice subsided.

On August 10, 20 c.c. of brominol was injected through the drainage tube under roentgenoscopic control. A roentgenogram immediately after the injection shows the stump of the cystic duct and the common duct well outlined. The common duct appears greatly dilated and the intrahepatic ducts appear dilated and blunted. No evidence of opaque medium in the small bowel is seen in this film. The roentgenogram made fifteen minutes later shows some scattering of opaque medium in the small bowel. A film made three hours later shows slightly more medium in the small bowel though the hepatic ducts and the common duct remain well filled.

Four days later clamping of the tube produced severe pain.

Two weeks later the tube came out spontaneously.

Four weeks later on September 24, 1934, the patient returned to the hospital markedly jaundiced and complaining of severe pain in the epigastrium and right upper quadrant of the abdomen.

The following day the patient was again operated upon. The common duct was greatly dilated and bound down with many obstructive adhesions. Some gravel was found in the duct. The pancreas was markedly infiltrated. The common duct was reconstructed around a T-tube. Convalescence was rather stormy. On the twelfth postoperative day, October 7, 1934, a brominol injection through the T-tube was made under roentgenoscopic control. The immediate roentgenogram showed marked dilatation of the common duct and dilatation and blunting of the intrahepatic ducts. The T-tube showed one short limb apparently outside of the common duct with some free opaque medium about the tube. No opaque medium was seen in the small bowel. Film made thirty minutes later showed no evidence of opaque medium in the small bowel.

About three weeks later, on October 31, 1934, the brominol injection was repeated with practically the same findings. At this time the patient was allowed to stand at the end of the injection and some opaque medium was seen to enter the duodenum. The patency of the common duct was not considered adequate and the tube was not removed.

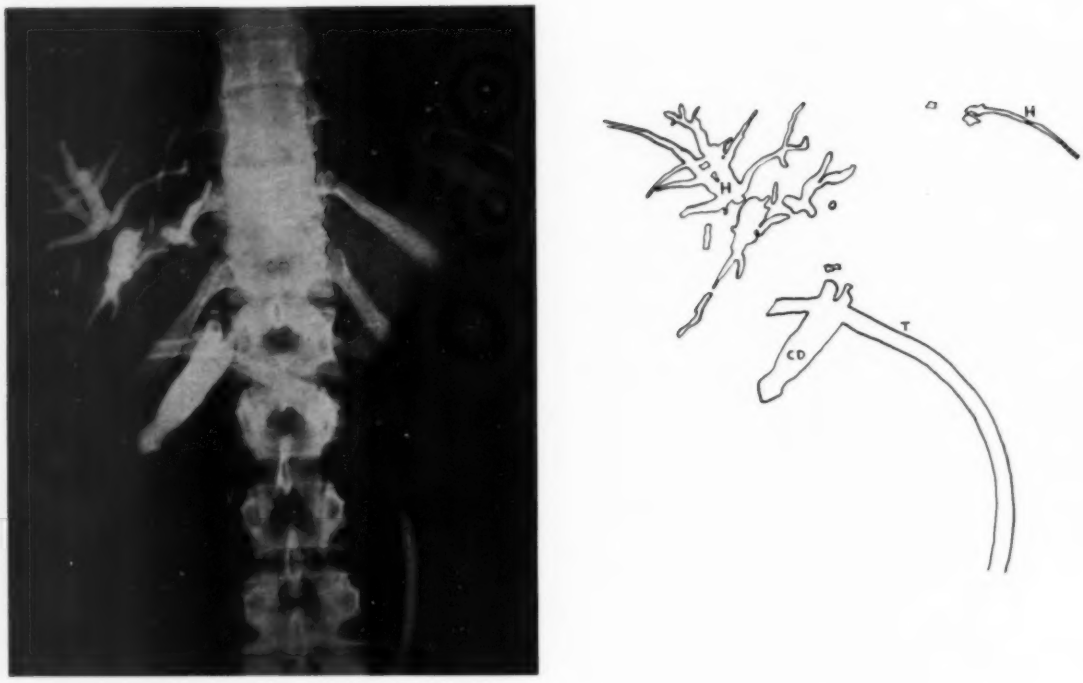

FIG. 8. Case V. *T*, T-tube one limb in common duct; *CD*, common duct dilated; *H*, hepatic ducts slightly less dilated. No opaque medium in small bowel.

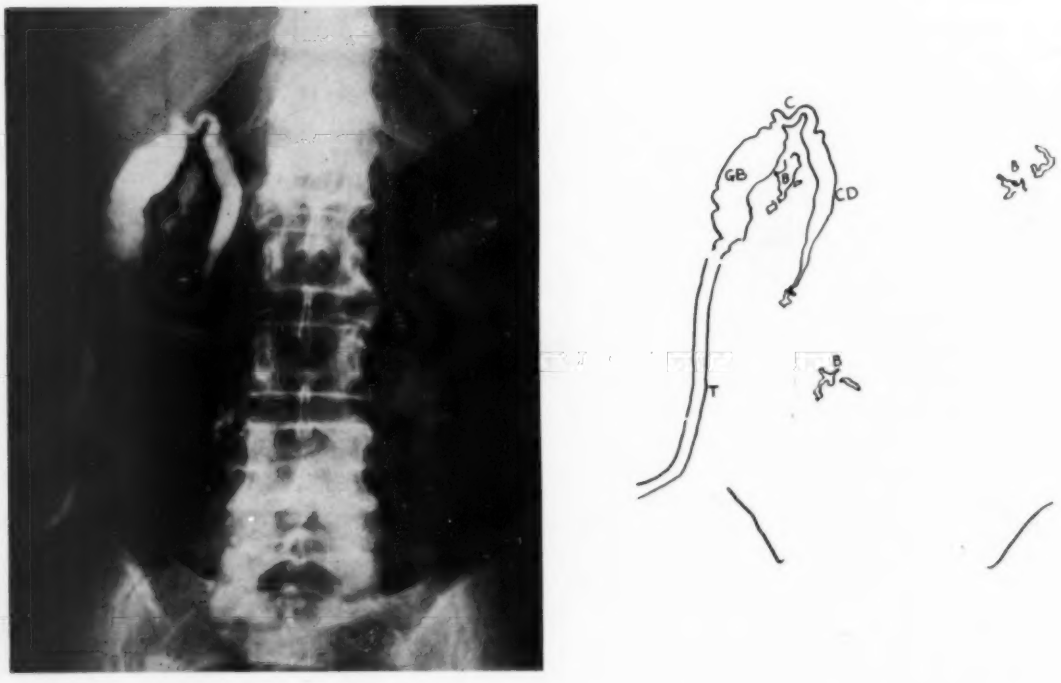

FIG. 9. Case VI. *GB*, gallbladder with drainage tube in fundus; *C*, cystic duct; *CD*, common duct dilated, some constriction at distal end; *B*, opaque medium in bowel, common duct patent.

Three months later, on January 25, 1935, the patient returned for re-examination. Similar findings were again present except for less evident dilatation of the intrahepatic ducts. No appreciable change appeared in the size of the common duct. No evidence of opaque medium was seen in the small bowel even in the roentgenogram made thirty minutes subsequent to the injection of the brominol. Patency of the common duct still not established.

Comment. This case is interesting from several angles:

(1) The long-standing history of seven years' duration foretells the findings that were observed at the operations and in the subsequent biliary tract visualizations. They are the findings of long chronic biliary system infection, viz., subacute cholecystitis with stones; dilated common duct with gravel; multiple adhesions with inflammatory glands about the duct and induration of the pancreas. The brominol injections tell a similar story. The dilated common duct, the dilated and blunted intrahepatic ducts and the repeated evidence of inadequate patency of the common duct all speak for long chronic biliary tract infection.

(2) The lack of patency of the common duct was evident at the first brominol injection, and in the light of the findings of this examination, it was very likely that a reoperation would be necessary when the drainage tube came out prematurely.

(3) The necessity for the T-tube even after a period of four months is made evident by the subsequent brominol injections. Removal of the drainage tube from the common duct may not be considered safe when there is not free passage of opaque medium into the duodenum under roentgenoscopic observation, or at least, evidence of medium in the small bowel in the roentgenogram made immediately subsequent to the injection. This fact is amply demonstrated in this case, and in Case III, as well as in several others in our series.

(4) The evidence of less dilatation of the intrahepatic ducts visualized in the roentgenograms made at the last examination would seem to indicate a definite improvement in the condition of the biliary tract. This conclusion has seemed to be warranted in this case as well as several others with prolonged drainage.

Case VI. Mrs. L. M., aged seventy-five. Patient entered St. Vincent's Hospital on May 20, 1932, complaining of severe pain under the right ribs that shifted both to the back and downward. There was no nausea, no vomiting, slight distention and no jaundice. Lack of appetite, general weakness, malaise and obstipation had been prominent symptoms for two years.

At operation under local anesthesia there was found a hydrops of the gallbladder with three gallstones present, one very large. Cholecystostomy. No exploration. Cultures of the bile and gallbladder wall were negative. The convalescence was uneventful. There was satisfactory drainage. On the eleventh postoperative day a brominol injection was made under roentgenoscopic control. The opaque medium was observed to pass freely into the duodenum. An immediate subsequent roentgenogram shows a well-filled gallbladder; a rather tortuous cystic duct, not dilated; a well-outlined common duct which appears narrowed near the distal end but is evidently freely patent with considerable opaque medium seen in the duodenum. The hepatic radicles are not visualized.

The drainage tube slipped out spontaneously on the twelfth postoperative day. Patient has remained well.

Comment. Brominol injection in this case made it possible to reassure the patient regarding the possibility of a remaining stone in the gallbladder or common duct even though the patient's condition at the time of operation would not permit of exploration. The continued health of the patient is proof of the worth of the brominol examination in this type of case.

CONCLUSIONS

The value of the information obtainable from this method of examination of the postoperative biliary tract would seem to recommend it for more general use in gallbladder and common duct surgery. It is by no means to be considered a substitute for the usual clinical methods of determining the course of the postoperative care of common duct drainage cases, but rather a valuable adjunct to these ordinary procedures.

The visualization of the common duct, giving accurate knowledge of its caliber, possible stones or strictures, and its patency, provides a sense of assurance to the surgeon which has been largely wanting in the past.

An early determination of these facts, made possible by a method which can in no way bring harm to the patient if the proper technique is used, will in many instances prevent the premature removal of the common duct drainage tube and obviate the probable necessity of reoperation. In the event that free patency of the common duct is determined early, hospitalization and drainage tube continuation may be definitely shortened.

Though too few cases have as yet been studied to arrive at absolute conclusions regarding the influence on prognosis by the various changes noted in the intrahepatic biliary duct system, certain facts seem evident.

To appreciate the changes resulting from pathology of the biliary tract, continued over a long or short period, one must first have some idea of the appearance of a normal biliary duct system. Opaque medium studies, in the human, of the normal living biliary tree are obviously impossible. However, the work of Counseller and McIndoe[3] with celloidin injections of the liver ducts made in fresh post-mortem specimens has given us excellent criteria for the normal as well as the pathological biliary tree. Study of their work will aid in forming some conception of the normal intrahepatic duct system injected with a radiopaque medium.

In cases with protracted biliary system infection, the variations evident in the hepatic ducts are marked and afford some estimate of the damage done to the hepatico-biliary structures in these infections. The practical application of this knowledge can only be increased by further study.

SUMMARY

1. The injection of a radiopaque medium such as brominol is a practical method of postoperative visualization of the biliary tract.

2. The development of the use of this medium is traced historically.

3. Technique of injection under roentgenoscopic control, the number of roentgenograms made and points to be watched in their interpretation are all outlined.

4. Six case reports are given from a series of forty-five in which radiopaque medium was used for the postoperative study of the biliary tract.

5. These six cases serve to illustrate the practical application of this type of examination in the various contingencies of biliary tract surgery.

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Vol. 37, No. 2

ROENTGEN KYMOGRAPHY CONSIDERED IN RELATION TO HEART OUTPUT, AND A NEW HEART INDEX

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THE single function of the heart is to pump the blood,[8] and the heart output is one of the most important constants of the body. Cardiac output determination, however, has failed to take the place it deserves in clinical diagnosis because of the difficulty of applying present methods to human subjects and because there has not been full confidence in the data obtained by some of the methods that have been employed. The dye injection method[6] and other methods recently developed or improved now show promise of giving a satisfactory degree of accuracy, but from the patient's viewpoint the technique is still rather formidable. There is definite need for an easily applied method of obtaining reliable data on heart output.

A number of investigators have turned to the roentgen ray for a possible solution of the problem. The literature on this subject is too extensive for review in this short communication, but the highest achievement in this field is represented by the extensive investigations of Bardeen,[1] Eyster and Meek,[2] and F. J. Hodges.[4]

None of the roentgen methods, however, has attained a position of practical utility. This is due, in large measure, to the complicated and expensive equipment required and to a wrong viewpoint or approach to the problem. The first difficulty was unavoidable with the older methods. The second requires explanation as it involves clarification of the objective of the roentgen method of approach. All roentgen methods so far attempted are based upon the measurement of the difference in the volume of the heart in complete systole and in complete diastole. This product has been spoken of as heart output which it obviously is not. Even if heart volume could be measured with a satisfactory degree of accuracy, the product would still not be stroke volume, although it might parallel stroke volume in normal individuals. At best, the roentgen method shows merely the changes in heart size, whereas beat output is the amount of blood actually delivered to the circulation. An engineer would not measure the outside dimensions or the movements of a water pump in order to determine its capacity but would measure the quantity of water delivered by the pump per stroke or for some unit of time or power. This is what heart output methods do with varying degrees of accuracy. Obviously the roentgen methods so far employed do not measure output, but merely the external movements of the pump. Failure to observe or sufficiently emphasize this fundamental difference in objectives of the roentgen and the true output methods has undoubtedly exercised a retarding influence on the development of the former. Cardiologists are not likely to accept a method which at its outset is based on a significant fallacy.

It may be asserted by some that the heart is not like the old farm pump with rigid cast iron walls but that it is more like a rubber bulb with inlet and outlet valves in which a reduction in volume of the bulb would be associated with a proportionate discharge of fluid at the outlet. This is true only in part. If the volume changes of one ventricle only could be measured accurately the analogy would probably hold, but not when the whole heart enters the computation, as the interior of the heart is complicated by septa and valves and the contraction does not occur simultaneously in all chambers. When the ventricle is at full systole the atria are already partly

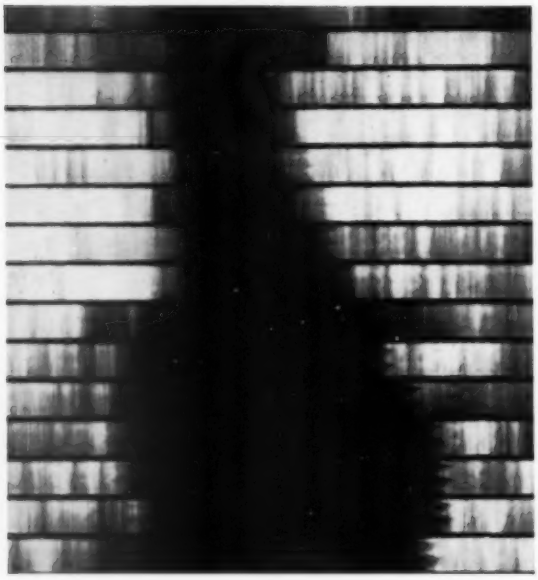


FIG. 1. Roentgen kymogram of Case 11, Table 1. Normal subject. The measurements derived from this kymogram have been transferred to the diagram, Figure 2.

filled. We have reason to believe that there is considerable movement of the intracardiac septa when external movement is restricted. In fact, there may be no detectable external movement of the ventricles in adhesive pericarditis,[5] and the output by the roentgen method would be zero. Since this would be incompatible with life, we appear to have proof that there is something going on in the heart that does not show on the surface.

As set forth above, we have objected to the older methods because of the necessary complication of equipment and because of the incorrect, or lack of clear, statement of the objective of the roentgen method.

The first difficulty may be removed by the substitution of roentgen kymography for the older technique. This method is as simple as ordinary chest roentgenography. The equipment occupies little space and need not be expensive. As to accuracy, we do not as yet have sufficient data to justify any positive statement. The 10 cases reported herewith show a fair degree of uniformity as compared with the dye injection method of cardiac output determination.

The second objection we attempt to meet with the frank assertion that the values we derive are not cardiac output. As we derive our values we intend them to represent as nearly as possible the extreme volume changes of the left ventricle. We wish to emphasize again that the method does not show beat output, but merely the external movement of the pump. The values derived should parallel beat output under normal conditions. In order to simplify discussion, we shall call our derived value, tentatively, the *roentgen kymographic heart index*. We believe that this simply derived index may be of value in some cases because it parallels beat output and, in other cases, because it deviates significantly from stroke volume.

METHOD OF COMPUTING THE ROENTGEN KYMOGRAPHIC HEART INDEX

All of the data required for computing the roentgen kymographic heart index are obtained from the roentgen kymogram (Fig. 1). As stated above, the object of the

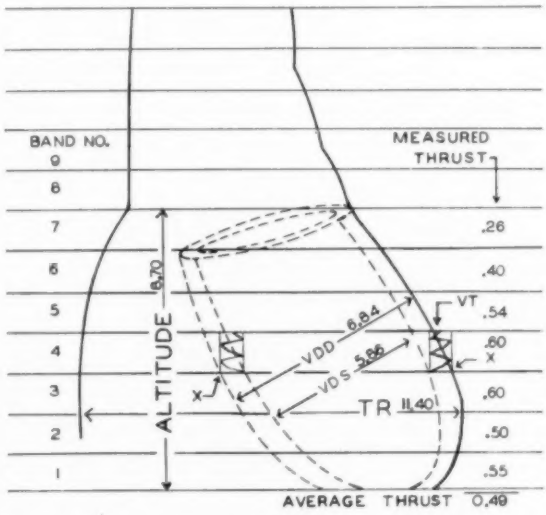


FIG. 2. Diagram illustrating the method of obtaining the roentgen kymographic index. The values shown are derived from the kymogram reproduced in Figure 1. *TR*, transverse diameter; *VDD*, ventricular diastolic diameter (0.60 of *TR*); *VDS*, ventricular diameter in systole (*VDD*–2*VT*); *VT*, ventricular thrust; *X*, point on heart border which produces thrust curve, indicated in band 4, only. Area of circle *VDD* – area of circle *VDS* × altitude = roentgen kymographic index—in this case 69.16.

method is to determine the extreme difference in volume of the left ventricle in complete diastole and complete systole. This difference is the roentgen kymographic index.

In deriving the index, three factors are obtained from measurements taken directly from the kymogram. The left ventricle is treated as a cylinder (see Fig. 2). From the measurements are estimated the length, diastolic and systolic diameters, of the cylinder. From these figures the two volumes are computed and their difference is taken as the kymographic index.

The average diameter of the ventricle in diastole (*VDD*) is estimated as 0.6 the total transverse diameter of the heart. The diameter in systole (*VDS*) is the diastolic diameter less twice the amount of the ventricular thrust (*VT*). The ventricular thrust is the mean obtained by measuring on the kymogram the amplitude of excursion of the left ventricle in all bands showing ventricular curves (bands 1 to 7, Figs. 1 and 2). These measurements are made very carefully with the aid of accurate and sharp-pointed dividers. The length of the ventricular cylinder is taken as the vertical altitude measured between the lowest and the highest bands that show the ventricular form of curve.

The factors for length and diastolic diameter are obviously tentative and may be modified by further experience. They were selected after comparable measurements on a considerable amount of dissecting room material.

The method of deriving the roentgen kymographic index is illustrated in Figure 2. The values shown in this diagram were obtained from the kymogram shown in Figure 1 (Case II in Table 1). The ventricular form of curve can be seen in bands 1 to 7, numbering upward from the left cardiophrenic angle. As explained in other papers on the subject of roentgen kymography,[9] the curve in each band is recorded from below upward. Each curve is, therefore, propagated from a single point on the heart border. This point is indicated by a cross (*X*) in band 4 of Figure 2. As an aid in measuring the ventricular thrust (*VT*) vertical lines may be drawn to indicate the positions of the troughs and peaks of the curves. If this is carried out in all of the bands, the stepladder character of the kymogram is clearly indicated.

The necessity of measuring ventricular thrust in more than one band may be questioned. We believe that it is desirable on theoretical grounds and have found it advantageous in practical application. In order to derive ventricular diameter in systole (*VDS*) it is necessary to subtract twice the amount of the average ventricular thrust (*VT*) from the ventricular diastolic diameter (*VDD*). The thrust of the ventricular walls must vary somewhat in different parts of the ventricle, especially the septal portion (see Morris-Jackson, Figs. 506 and 507),[7] and there is some distortion of curves where the heart border shows considerable curvature. It is hoped that these undeterminable factors will be at least partly corrected by using average thrust in our computation rather than the thrust shown in a single band. There is some doubt concerning the movement of the septum during ventricular contraction, but the structure of the ventricular myocardium[7] leads us to believe that the effect can be little more than a slight shortening of systolic thrust. There is some foreshortening of measured thrust in the upper bands of the kymogram due to the usual incurving of the upper ventricular border. We believe that averaging these low values with those of the lower bands serves as a corrective factor for the diminished thrust of the interventricular septum.

Computation of the roentgen kymographic index may be expressed briefly in the following equations, bearing in mind that transverse diameter, altitude (*ALT*) and ventricular thrust are obtained by direct measurement from the kymogram:

$$0.6\ TR = VDD$$

$$VDD - 2VT = VDS$$

Then area $\bigcirc VDD$ − area $\bigcirc VDS \times ALT =$ *RKG* index.

An alternate method in which the area of ventricular movement on the left border of the heart is measured with a planimeter and multiplied by the factor representing ventricular diameter may be employed. The results obtained with this method have not been as consistent as with the method outlined above.

Table I

Case	Diagnosis	Date	Blood Pressure	Stroke Volume[1]	*RKG* index	*SV*/*RKG* index	*RKG* index / *SV*
I	Normal	7- 3-35		146	137	1.0	0.93
II	Normal	7-19-35	110/70	85	69.16	1.2	0.95
		7-22-35		96	92	1.0	0.95
III	Normal	7- 9-35	124/80	81	77	1.05	0.95
		7-13-35[2]	140/84	130	113	1.15	0.87
IV	Normal	7-16-35	120/75	92	88	1.04	0.95
		7-18-35[2]		100	71	1.40	0.71
V	Hypertension	7- 8-35	220/140	80	81	0.98	1.01
VI	Hypertension	7- 5-35	230/110	111	119	0.92	1.07
VII	Hypertension	7- 1-35	200/120	101	114	0.88	1.12
VIII	Malignant hypertension	3-21-35	240/150	23	51	0.45	2.21
IX	Rheumatic	7- 2-35	120/75	76	240	0.31	3.15
X	Adhesive pericarditis	5-21-35		88	231	0.38	2.62
	Average of all cases			92	114		
	Average excluding Cases IX and X			94	92		

[1] Kinsman and Moore.

[2] After digitalis.

Roentgen Kymographic Index Compared with Stroke Volume

Through the cooperation of Drs. John Walker Moore and J. Murray Kinsman we have had the opportunity to compare the roentgen kymographic index with stroke volume determinations made by the dye (brilliant vital red) injection method in 10 patients. In each case the kymogram was made at the same time as the stroke volume determination. Four patients exhibited no evidence of cardiovascular disease and were regarded as normal. Three were compensated cases of hypertension, one a case of malignant hypertension, one a rheumatic with mitral stenosis and insufficiency, and one a case of adhesive pericarditis in good condition five months following partial removal of the adherent pericardium. The essential data on these cases are given in Table I.

In Figures 3 to 10 are shown a series of

single ventricular bands from cases listed in Table 1 and an additional normal case.

Figure 3 is from Case 1, and is characterized by deep thrust, high stroke volume, high roentgen kymographic index and slow heart rate.

Figures 4 and 5 are from Case III, before and after digitalis. The second curve shows a slightly deeper thrust, a shortened period of rapid filling and consequent prolongation of the period of slow filling. The average thrust before digitalis is 0.46, following digitalis, 0.55.

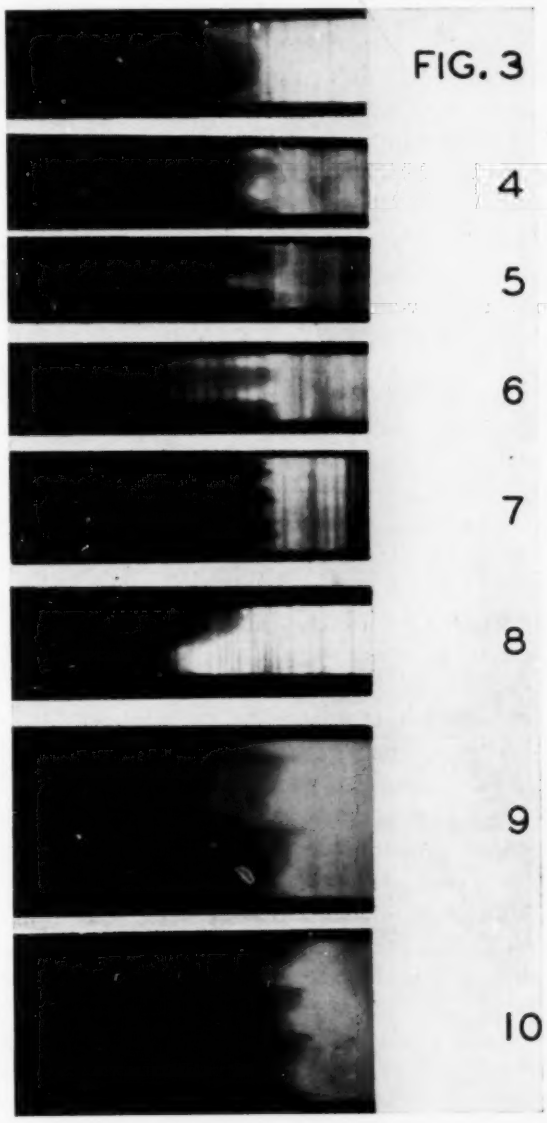
Figure 7 is from the kymogram of Case VIII, malignant hypertension. Thrust is greatly diminished (average 0.22) and the curve form is decidedly abnormal. The roentgen kymographic index is down, but not nearly so much as stroke volume. The difference may have been caused by augmented heart action resulting from placing the patient in the erect position for the roentgen exposure.

Figure 8, Case IX, shows the wide thrust of mitral regurgitation. The kymogram shows an average thrust of 0.62 with variation in different bands from 0.36 to 0.90. The patient was well compensated and had a stroke volume of 76. The high roentgen kymographic index of 240 may indicate the amount of blood that reaches the ventricle during diastole and if that is the case the roentgen kymographic index less stroke volume would represent the amount of blood regurgitated through the leaky valve.

Figures 9 and 10 are from a wide-grid kymogram and show ventricular curves of a normal subject before and after mild exercise. Roentgen kymographic index before exercise, 65.51, after exercise, 59.54. Substituting these values for stroke volume and multiplying by heart rate, the minute volume would be 4.84 liters before, and 5.59 liters after, exercise. We have no output data on this subject.

In comparing the figures in the last four columns of the table several interesting features may be observed.

First, in comparing the stroke volume with the roentgen kymographic index,



Figs. 3 to 10. Single ventricular bands from kymograms of cases listed in Table 1 and an additional normal subject. See text.

omitting Cases IX and X which had mechanical impairment of heart action, it is seen that the average beat output by the dye injection method is 94 c.c. and the average roentgen kymographic index is 92. There is, however, considerable scattering in individual cases. It is reasonable to expect improvement of results with more exact technique. Methods of determining heart output are subject to error and in evaulating the kymographic index it is

well to keep in mind the fact that we have no absolute values to use as a basis of comparison. Available data must be used, however, in establishing the significance of the kymographic index. The logical and proper procedure would be to make the kymogram and the output determination at the same time under the same basal conditions. There would be no point in comparing data on another, or even the same, subject under different conditions.

Case IX is of special interest. This patient had auricular fibrillation, mitral stenosis, and marked insufficiency of the mitral valve. The output was 76 and the roentgen kymographic index 240. The index in this case may be of value as an indication of the degree of the valvular defect and of the additional load put on the heart in order to maintain adequate circulation. Stated in other words, the left ventricle is pumping a larger volume of blood than that which reaches the circulation. This shows in the kymogram, but not in output values since output methods measure the amount that reaches the pulmonary or general circulation, while the kymogram shows the amount of ventricular contraction. As an index of valvular insufficiency, therefore, the kymogram may have a significance and value not possessed by the output determination alone.

Case X also shows a high kymographic index with essentially normal output. Here the high index cannot be explained on the basis of valvular insufficiency as there was no evidence of valvular defects. The explanation is probably to be found in the fact that only a part of the adherent pericardium was removed and that the freed portion of the ventricle overworked to compensate for the mechanically hampered portion.

Cases IX and X show that ventricular thrust may be out of proportion to output under certain conditions and further emphasize our reasons for objecting to the term output so far as roentgenographic methods are concerned.

In columns 7 and 8 we have included a series of figures the significance of which we shall make no attempt to evaluate. Perhaps they have none, but in our small series of cases the numbers vary in a manner which suggests that they may be of value as an index of the relative efficiency (column 7) and relative effort (column 8) of the heart.

The numbers in column 7 are the product of the stroke volume divided by the roentgen kymographic index. As would be expected, this number is unity or near unity in the normal cases. It diminishes slightly in the cases of benign hypertension and very markedly in Cases VIII, IX and X, all of whom had grave cardiac disease.

If we may, for the moment, regard this quotient as an index of efficiency, it follows that Case VIII has a cardiac efficiency index of 40 per cent, and Case IX, 31 per cent. We have no idea as to how closely these figures would correspond with accurately measured cardiac efficiency. The stroke volume and the roentgen kymographic index represent entirely different, but necessarily related, actions of the heart. Stroke volume, as the name implies, is the amount of blood actually thrown into the circulation, whereas the roentgen kymographic index represents the amount of movement required of the ventricle in order to deliver the given quantity of blood to the circulation. It appears possible, therefore, that the new factor, SV/RKG, may furnish useful data on heart action which has not hitherto been available.

Before leaving column 7, it is of interest to note that two of the normal patients showed a slight increase in the "efficiency index" under digitalis.

The numbers in column 8 are obtained by dividing the roentgen kymographic index by the stroke volume. If we may assume for the moment that this factor represents relative heart effort, we observe that effort is diminished in the 2 normal cases following digitalis, increased slightly in hypertension, doubled in the case of malignant hypertension, and tripled in the case of advanced rheumatic heart disease with gross mitral insufficiency.

DISCUSSION

In the observations reported above there are certain apparent technical defects. Distortion is not corrected by the best method. The left ventricle is treated as a chamber of cylindrical contour which is not strictly the case, and the factors used to represent diameter and length of the cylinder are not absolute. Further, the patients in our series were not in strictly basal condition at the time the kymograms were made. We recognize the importance of these defects but feel encouraged by the results obtained under difficult conditions.

In our new setup the matters of distortion and of having the patient in basal condition will be corrected. The kymograms will be made at 2 meters, at the same time as the output determination and without disturbing the patient in any way. In the observations reported herewith distortion is at least partially corrected in the selection of the factor to represent the diameter of the ventricle. This factor will be modified somewhat for films made at 2 meter anode-film distance.

As to the shape of the left ventricle, it probably resembles a truncated cone more closely than a cylinder. However, we believe that the best we can hope for in the selection of the diameter factor is a number that has relative value and for that reason have chosen a factor which is a function of total transverse diameter. Whether or not this will prove satisfactory in cases of cardiac hypertrophy, we do not know, as there are no available data on this point. We believe that this method will prove more satisfactory than that of using the whole cardiac silhouette.

Our factor for length of the ventricular cylinder is also relative with slight foreshortening due to the obliquity of the long axis of the ventricle as related to the longitudinal axis of the body. The advantage of using a vertical line for this factor instead of an oblique line is due to the fact that we have fixed points on the kymogram between which the measurement is made. If an oblique line were projected from the apex there would be no way of knowing where to end the projection superiorly.

It will now be apparent to the reader that we do not regard our method of determining ventricular volume as ideal or of absolute value. It is quite improbable that this volume can be determined with anything like a high degree of accuracy. The estimates should be regarded as relative and not absolute. It is probable that errors will be repeated in fairly proportionate ratios. The value of the roentgen kymographic index rests upon this assumption.

Bardeen's[1] method of computing heart volume might, of course, be applied to the kymogram. We believe, however, that its application to the kymogram would be subject to greater error than the method we have employed and that the error factor would probably not be repeated in as constant a ratio. So far as the kymographic index is concerned, the actual amount of error loses much of its significance if it is repeated uniformly and consistently. Our objection to Bardeen's method is that it includes the atria and roots of the great vessels, the contractions of which are not simultaneous with ventricular contraction, and in pathological conditions, may not be synchronous. The essential contraction is that of one or the other of the ventricles. Inclusion of other parts of the heart borders merely increases the possibility of error. Further, the stepladder character of the kymogram makes accurate planimetry very difficult.

In conclusion, we wish to emphasize again our position that the roentgen kymographic index should not be used as a substitute for beat output. The former shows the movements of the pump whereas the latter shows the output. We believe that, with refinements in technique, the former will prove to be a useful index of the latter, in the absence of mechanical interference with heart action such as an adherent pericardium or defective valves. In the absence of such defects, the kymographic index should parallel beat output and, in their

presence, may be of value as an index of the extent of impaired function. The method should find other uses as, for example, the study of the effect of various agents on the action of the heart muscle and the effect of exercise, rest and fatigue.

The method should be applied with full understanding that it shows ventricular movement, not output, and that it is subject to certain unavoidable limitations. It is recommended by simplicity of application and by the fact that it makes available data on heart action that cannot be obtained by any other method.

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A ROENTGENOLOGIC STUDY OF THE SHIFTING OF BLOOD IN THE CIRCULATORY SYSTEM OF EXPERIMENTAL ANIMALS UNDER THE INFLUENCE OF VARIOUS STIMULI

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THE shifting of blood in the circulatory system has been for many years the object of considerable study. This study has been accomplished mainly by means of plethysmographic methods from which much valuable information has been obtained. However, the data thus collected apply only to the selected vascular area or areas which were the object of observation.

In order to be able to study the shifting of blood to and from all the areas of the circulatory system at the same time, we have made the blood of experimental animals radiopaque. This was accomplished in non-anesthetized rabbits by withdrawing about one-fourth of the blood from the heart and immediately restoring the blood volume to the original level by injecting an equal amount of thorium dioxide sol in one of the ear veins. This procedure, which is only a generalization of clinical arteriography,[1,2,7] gives an excellent visualization of all vessels with a diameter greater than 0.2 mm.

Roentgenograms of animals prepared in this manner, taken in the anteroposterior position, show more clearly the vessels of the neck, those of the limbs, the pulmonary vessels and the vessels of the kidneys. The lateral position is preferable to show the aorta in its entire length, the interventricular septum of the heart, the inferior vena cava, the suprahepatic veins, the celiac trunk and the portal system. The cerebral vessels, due to the thickness of the skull and its complicated structure, escape investigation in the rabbit but it is likely that in other animals with less skull and more brain, the vessels of this important area could also be visualized.

The opaque medium does not remain in the circulating blood permanently but its granules are rapidly phagocytized by the cells of the reticulo-endothelial system. In 3 rabbits, in order to observe the rate of disappearance of the blood opacity, serial roentgenograms were taken at five minute intervals during one hour after the injection of thorium dioxide. For the first ten minutes most of the thorium could be seen in the circulating blood; at the fifteenth minute the spleen began to acquire some opacity and at the twentieth minute the liver also became opaque while the blood appeared somewhat more transparent. Up to this time no changes could be observed in the shape or diameter of the vessels in any of our animals. One hour after the injection, the medium had completely disappeared from the circulating blood and had accumulated in the liver and spleen. In these rabbits as well as in those used in successive experiments the disappearance of thorium from the blood coincided with a decrease in vitality. While during the first hour they had behaved in a perfectly normal manner, later they became progressively less active and all of them died between the third and fourth hours following the injection of thorium.

We were unable to establish the cause of their death. At autopsy the lungs, heart, intestine, muscle, brain and kidneys were found grossly and microscopically normal but the cells of the reticulo-endothelial system, and especially those of the liver and spleen were literally choked with granules of thorium dioxide. The hypothesis of an acute blockage of the reticulo-endothelial system is highly speculative.

During the first twenty-five minutes following the injection of thorium the blood pressure in the carotid artery was studied in 3 rabbits under ether anesthesia. Im-

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A *B* *C*

FIG. 1. *A*. Soon after injection of thorium dioxide (1 = carotid artery, 2 = jugular vein, 3 = superior vena cava, 4 = aorta, 5 = right ventricle, 6 = left ventricle, 7 = pulmonary vessels, 8 = suprahepatic veins, 9 = inferior vena cava, 10 = portal vein). *B*. Soon after the intravenous injection of 2 c.c. of histamine. *C*. Two minutes later.

mediately after the withdrawal of blood, the pressure fell sharply but it was restored to the previous level by the injection of thorium which brought the blood volume back to the original amount. Fairly constant pressure was maintained for about fifteen minutes, then a slight and gradual fall was observed.

This preliminary study shows that in spite of the fact that the method used was always ultimately fatal to the experimental animals, no appreciable effect could be detected on their general behavior, on the size or shape of their vessels or on the blood pressure as long as most of the opaque medium could be seen in the circulating blood. We think, therefore, that at least during the first fifteen minutes following the injection of thorium, we were dealing with essentially normal experimental subjects. In order to have an extra margin of safety, all the experiments later described were completed within the first five minutes after the visualization of the blood.

In all the following experiments, two preliminary roentgenograms were taken as controls soon after the injection of thorium. Various stimuli were then applied to the animals and the effect upon the circulatory system was followed with other roentgenograms taken at rapid intervals. For each experiment at least 3 animals were used. Most roentgenograms were taken in a lateral position because this gave us a better visualization of the most important structures. The animals were securely but comfortably tied to a holder.

After visualization of the blood we studied the effect of histamine, ephedrine, adrenalin, air embolism, oil embolism, fracture of the skull, position, hemorrhage, pituitrin, ether anesthesia, asphyxiation, electrocution, and increase in blood volume. From these experiments we have selected only the first eight as being more representative of the various types of vascular reactions.

The intravenous injection of a lethal dose

A *B* *C*

FIG. 2. *A*. Soon after the injection of thorium dioxide. *B*. Soon after intravenous injection of 1.5 c.c. of ephedrine. *C*. Three minutes later.

of histamine (usually 2 c.c.) decreases the volume of the systemic and pulmonary arteries, dilates the veins of the systemic circulation, congests the liver, reduces the size of the left ventricle and increases the filling of the right ventricle (Fig. 1). All our animals died within four minutes after the injection of the drug.

We know that one of the most striking characteristics of histamine is the immediate fall in blood pressure. It has also been conclusively proved that histamine increases the permeability of the capillary walls,[4,5,6] thus inducing a loss of blood volume. In our animals a marked fall in pressure was observed soon after the injection of the drug, but we cannot explain it on the basis of the loss of blood volume because in the roentgenograms the fullness of the veins and the congestion of the liver more than compensates the small volume of the arteries. But if we consider the striking decrease in the size of the left ventricle and the dilatation of the right ventricle and if we consider how small the pulmonary arteries have become we can explain this picture on the basis of a sudden contraction of the pulmonary area.

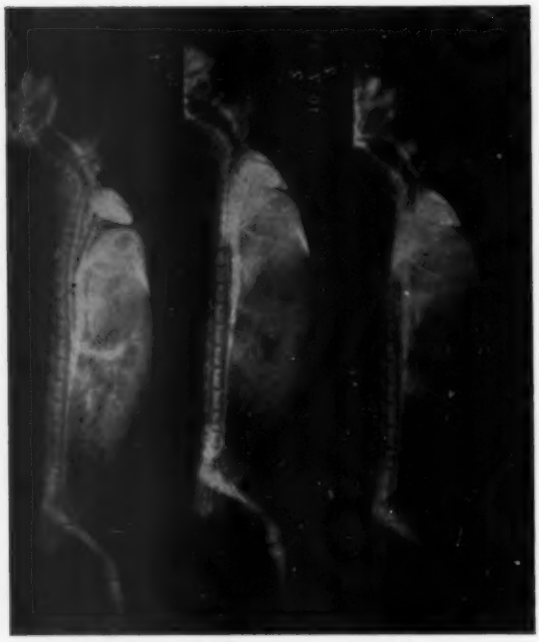
A *B* *C*

Fig. 3. *A*. Soon after the injection of thorium dioxide. *B*. Soon after the intravenous injection of 1 c.c. of adrenalin. *C*. Five minutes later.

A *B* *C*

Fig. 4. *A*. Soon after the injection of thorium dioxide. *B*. Soon after the rapid intravenous injection of 8 c.c. of air. *C*. Two minutes later.

The intravenous injection of a lethal dose of ephedrine (usually 3 c.c.) induces a most marked reduction in the volume of all systemic arteries, the systemic veins are greatly distended, and the liver is quite congested. These reactions are quite similar to those induced by histamine, but while histamine contracts the vessels of the lung and decreases the size of the left ventricle, after ephedrine the pulmonary vessels are greatly distended, the left ventricle has increased in volume, the right ventricle has also increased in volume although not as markedly as the left (Fig. 2). The animals died within five minutes after the injection. In this series of roentgenograms, we can note stasis and dilatation of all structures back of the aorta. The dilatation of the left ventricle makes it appear that the heart is trying to push the usual amount of blood through a much smaller aorta. We believe that the changes observed can be explained by a primary contraction of the large systemic arteries.



A *B* *C*

FIG. 5. *A*. Soon after the injection of thorium dioxide. *B*. Soon after the injection of 2 c.c. of lipiodol into the right ventricle. *C*. Two minutes later.

The intravenous injection of 1 c.c. of adrenalin induces a most marked dilatation of the aorta and large arteries. The pulmonary vessels are also dilated, the systemic veins small, the portal system less full of blood (Fig. 3). We can explain this picture on the basis of a contraction of the arterioles with the blood backing up into the arteries.

The inhalation of 1 capsule of amyl nitrate makes the left ventricle smaller, increases the diameter of the aorta and the other systemic arteries. The portal system contains considerably more blood. The systemic veins are slightly less distended. This picture could be explained by the active dilatation of the arterial walls, which allows more blood to collect in the arterial side of the circulatory system.

The rapid intravenous injection of 8 c.c. of air will induce a marked decrease in the diameter of the aorta and other arteries, and a distention of the systemic veins. The pulmonary vessels do not show appreciable changes (Fig. 4). As a quantity of the air is collected in the cardiac cavities these findings could be explained by an impaired heart function with decreased cardiac output. All animals died within three minutes following the injection of air.

The injection of oil (lipiodol) into the right ventricle shows that oil collects in the pulmonary vessels obstructing them. This induces a reduction in the size of the left ventricle, of all arteries, and a distention of the systemic veins. The pulmonary arteries are made more prominent, the right ventricle dilated, and there is interstitial hemorrhage in the lungs (Fig. 5). All animals died within three minutes following the injection.

Fracture of the skull does not always give the same circulatory reaction. In one animal immediately after the fracture we were able to observe a disappearance of blood from the whole body except the lungs which were greatly distended. This can be explained only by a contraction of both the systemic arteries and veins. In two other animals, immediately after the fracture, the aorta became enormously dilated and

A *B* *C*

FIG. 6. *A*. Soon after the injection of thorium dioxide. *B*. Soon after skull fracture. *C*. One minute later.

tortuous while the veins decreased in volume. One minute later a decrease in diameter of all the systemic arteries was observed. The pulmonary vessels were not overdistended (Fig. 6). It is possible that an explanation of such diverse reactions could be found in the different ways the vasomotor center was stimulated by the different fractures.

Upright position has a most marked effect upon the circulatory system of the rabbit as the blood tends to collect in the most dependent parts of the body.

Hemorrhage empties the heart and the arteries in the same degree as the veins; however, the abdominal vessels empty before the rest of the circulatory system.

DISCUSSION

The results of the experiments described above point to the fact that the circulatory system readily responds to various stimuli with diverse reactions. These reactions are not confined to the capillaries or arterioles of the systemic circulation but seem to involve every anatomical structure connected with the circulation of the blood.

Our experiments also show that the roentgenologic study of the shifting of blood has limitations and advantages. Among the limitations must be mentioned the fact that this method does not give any information concerning vessels with a diameter less than 0.2 mm. Therefore arterioles and capillaries, very important units of the circulation, cannot be visualized and it is only by inference that their condition can be estimated. Another important limitation is the lack of absolute volumetric measurement of the amount of blood in a given area. An estimate of the changes in the volume of blood in a certain territory can only be obtained by comparing the successive roentgenograms with the first ones. A third limitation is to be found in the fact that all experiments should be completed within fifteen minutes after the injection of thorium in order to avoid an excessive absorption of the dye by the reticulo-endothelial system. On the other hand, the advantages of the method consist in the possibility of examining all the visible vessels of the body at the same time. This naturally allows an evaluation of the shifting of blood which would be technically impossible with plethysmographic methods.

SUMMARY

In experimental animals, the withdrawal of about one-fourth of the blood volume, followed by intravenous administration of the same amount of thorium dioxide sol, allows the roentgen visualization of all vessels with a diameter of more than 0.2 mm.

This procedure is always ultimately fatal but during the first fifteen minutes no changes occur in the behavior, in the blood pressure or in the size of the vessels of the experimental animals.

The effect of certain doses of histamine, ephedrine, adrenalin, of air and oil embolism, of fracture of the skull, of hemorrhage, and of position, on the circulatory system, was studied in rabbits prepared by this method by means of serial roentgenograms.

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CONTRALATERAL BRONCHIAL INFECTON IN PULMONARY TUBERCULOSIS*

A STUDY OF 242 CASES

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IN STUDYING certain cases of pulmonary tuberculosis it was noted that tuberculosis of one lung was not infrequently complicated by what appeared to be a more recent infection of the opposite lung. The occurrence of a new infection in the left lung derived from an older lesion in the right lung was noted and described by Cole and others[1] in 1930. They applied the term "cross infection" to this phenomenon. The new infection would seem to be autogenous and is due apparently to the aspiration of infectious exudate and detritus from a bronchus of the earlier affected lung to that on the opposite side.

MATERIAL

This report covers the study of 242 selected cases of pulmonary tuberculosis and several experiments on non-tuberculous subjects and is intended to show that there exists in either lung a site of predilection for what we prefer to call "contralateral bronchial infection."

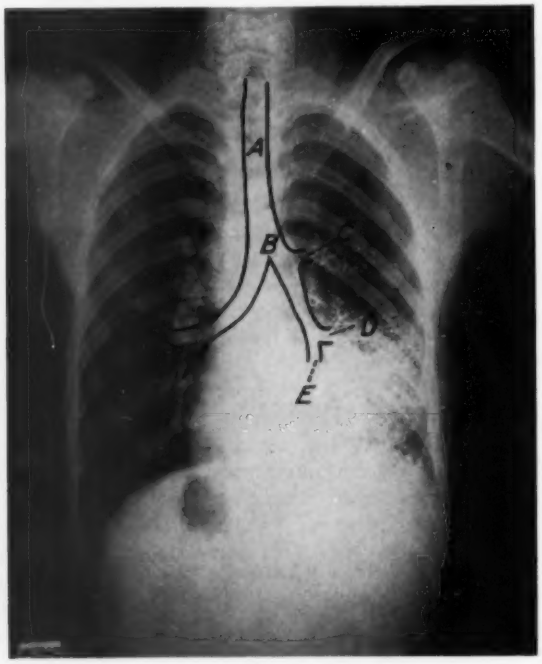

FIG. 1. Illustrative bronchogram.

ANATOMICAL STUDY OF BRONCHIAL DISTRIBUTIONS

The anatomy of the bronchi of the first and second order was studied by means of lipiodol injections of the bronchial tree (see Fig. 1). It is to be noted that the carina (*B*), the vertical partition that makes the bifurcation of the trachea, will permit of the free exchange of a fluid or semifluid exudate from the main bronchus of either side to the main bronchus of the opposite side. The right upper lobe bronchus (*C*) enters the side wall of the stem bronchus almost at its origin and directly opposite the carina. About 1½ inches below this the stem bronchus divides to form the main bronchus to the middle lobe (*D*) and that to the lower lobe (*E*).

The left stem bronchus is longer and divides about 2 inches from the carina to form the main bronchus of the upper lobe (*F*) and that of the lower lobe (*G*).

These differences especially as they concern drainage from and distribution to the upper lobes are important in deciding the site of intrabronchial cross infection. It is possible of course that cross infection may occur at any site in the contralateral lung, but our observations have enabled us to demonstrate that either lung has an area of predilection in which cross infection may be expected to occur. For the *right lung* this area corresponds to the third of the lung lying midway between the apex and the upper margin of the middle lobe. In roentgenograms taken in the usual posteroanterior projection this is found to lie in the *second* anterior interspace area. The

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site of predilection, however, for the *left lung* comprises one-fifth of the lung field midway between the apex and the base, and in roentgenograms corresponds to the *third* anterior interspace. At some spot within these areas early cross infection should be looked for, and it is frequently found that the whole of the selected areas is diseased.

gram shown in Figure 3 was then taken with the subject standing. It is readily seen that this short period of time has been enough to allow some of the lipiodol to pass from the right lower bronchial tree to enter the left main bronchus and to be distributed (*B*) through the smaller bronchi in the lower part of the left upper lobe —the area of predilection, seen in the roentgenogram to be in the third anterior interspace area. The subject of the experiment then lay on

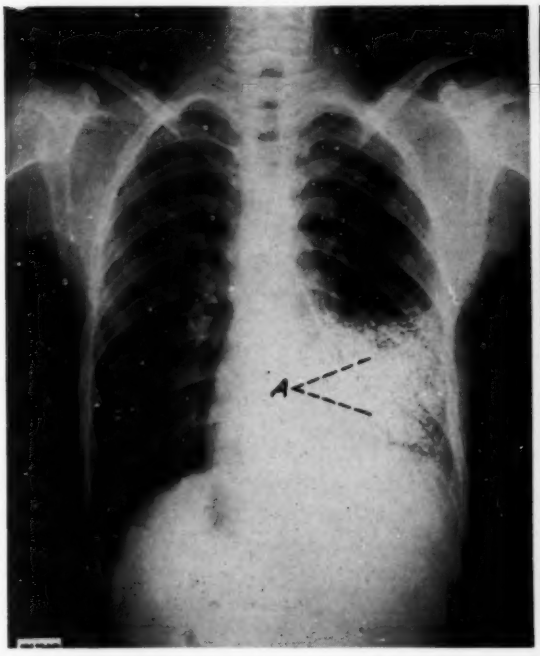

Fig. 2. Experiment 1.

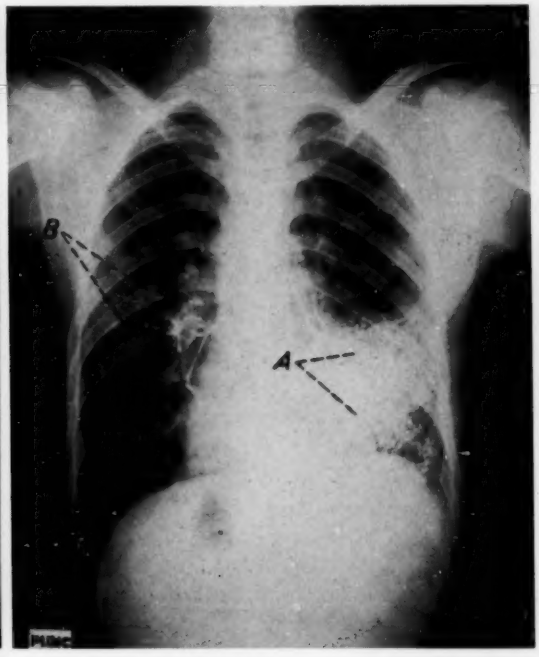

Fig. 3. Experiment 1, continued.

Bronchographic Studies in Non-Tuberculous Individuals

That oily solutions pass readily from the lung across the carina to enter the area of predilection in the opposite lung was demonstrated by the bronchographic study of 8 non-tuberculous individuals after the instillation of lipiodol into one or the other lung. Three experiments are selected for description.

Experiment 1. Ten cubic centimeters of lipiodol was instilled by the method of passive aspiration into the bronchial system of the right lower lobe of a healthy young adult. Figure 2 shows the situation (*A*) of this oily suspension, and that the left lung contains no oil. The subject of the experiment thereafter lay on his left side for five minutes and was encouraged to cough gently. The roentgenogram reproduced in Figure 4 was made in the upright position. It is now seen that the lipiodol has passed from the left lung to enter the right upper bronchus and is distributed in the area of predilection of the right lung (*C*) and lies under the second rib and in the second interspace area.

Experiment 2. The subject of this experiment had a somewhat marked cylindrical bronchiectasis of the left lower lung. The diseased bronchi were filled with lipiodol as shown in Figure 5. After lying on his right side for five minutes the patient was again roentgenographed in the upright position, with the result shown in Figure 6. Lipiodol had again passed freely from the left lower lobe to enter the right upper lobe and to be distributed to the smaller bronchi in the area of predilection.

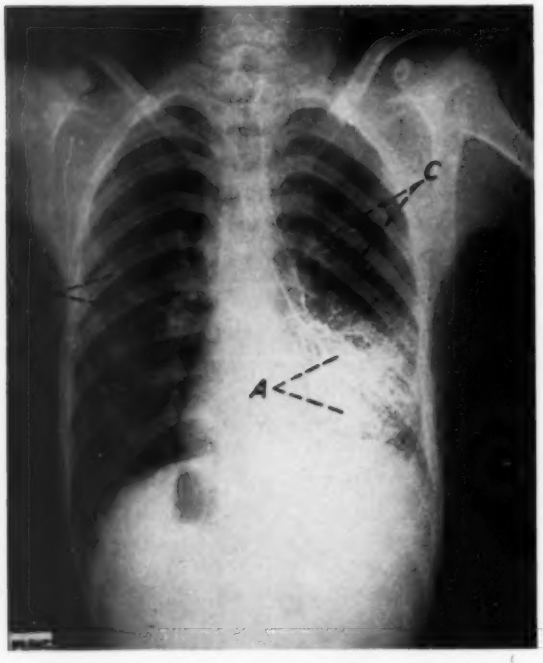

FIG. 4. Experiment 1, continued.

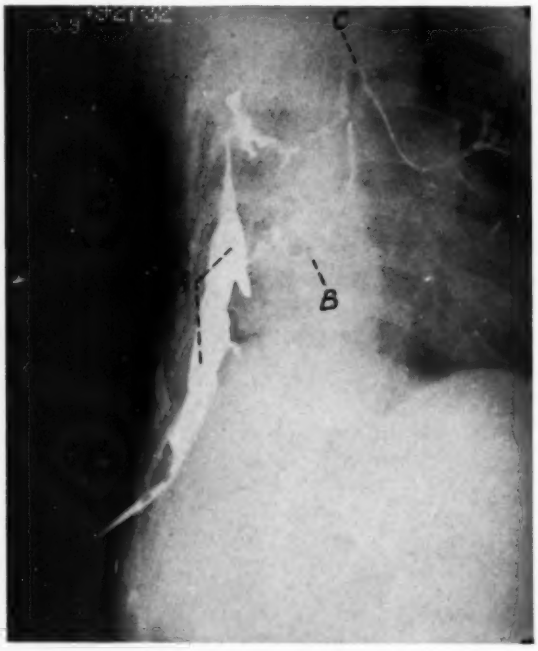

FIG. 7. Experiment 3.

Experiment 3. This was performed on a patient suffering from a right-sided chronic empyema with a bronchial fistula. With the patient lying on his left side 10 c.c. of a 12.5 per cent solution of sodium iodide was run into the empyema cavity (*A*, Fig. 7). Some of this watery solution entered the right lower bronchus (*B*) through the fistula, and after passing the carina (*C*) entered the left upper bronchus and was finally distributed through the smaller bronchi of the area of predilection of the left lung (*D*).

ROENTGENOLOGICAL AND CLINICAL STUDIES IN PULMONARY TUBERCULOSIS

All the chest roentgenograms taken by the Department of Radiology of the Peiping Union Medical College between the years 1922 and 1934 (about 20,000 in num-

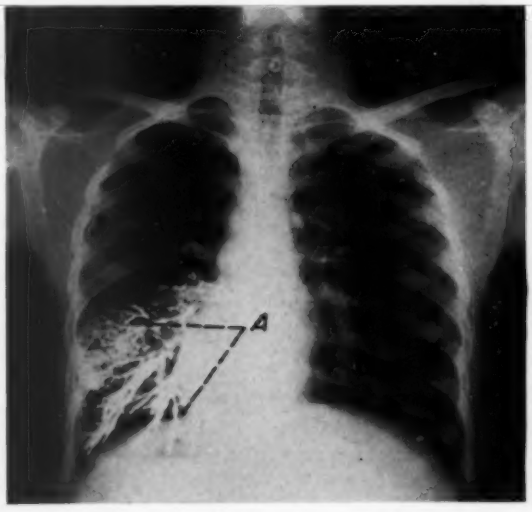

FIG. 5. Experiment 2.

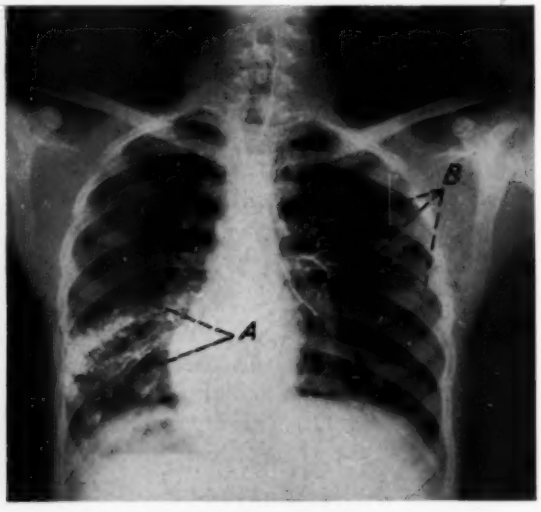

FIG. 6. Experiment 2, continued.

ber) were examined for evidence of contralateral bronchial infection. The phenomenon was found to be present in some 500 instances. From this number 242 cases were selected for special study on the basis of the availability of adequate clinical records. Twenty-two cases are of special interest in that at the time of the first roentgen examination one lung was found to be free from roentgenological evidence of tuberculosis, whereas at subsequent examinations contralateral bronchial infection was found to have occurred. Roentgenograms and short clinical notes on 8 of these cases are included in the report of illustrative cases. The findings, which do not merit prolonged description, are summarized in Tables I and II.

The following points are apparent and worthy of attention:

(1) That infection may pass from the left lung to the right as well as in the opposite direction.

(2) That cough and sputum were present in the majority of cases.

(3) That in almost 90 per cent of instances a cavity existed in the primarily affected lung.

(4) That in more than 90 per cent of the cases in which it occurred, contralateral infection was found in the second interspace area of the right side and the third interspace area on the left side—the areas of predilection.

(5) That physical signs were recorded in the secondarily infected lung in less than 50 per cent of the cases.

TABLE I

CLINICAL AND ROENTGENOLOGICAL FINDINGS IN 22 SELECTED CASES OF BILATERAL PULMONARY TUBERCULOSIS IN WHICH ONE LUNG HAD PREVIOUSLY BEEN KNOWN TO BE HEALTHY

Case	Age yr.	Clinical Symptoms			Physical Findings in Secondarily Involved Lung	Tubercle Bacilli in Sputum	Roentgen Findings										Secondarily involved lung
							Location of lesion								Cavity		
							Right*				Left*						
		Cough	Temperature	Sputum			1	2	3	4	1	2	3	4	Single	Multiple	
I	23	+	37°–38°C.	+	Fine râles	+		+			+	+	+	+		+ (L)	Right
II	29	+	Normal	?	Moist râles	+	+	+	+			+	+			+ (R)	Left
III	15	+	37°–38°	+	None	o	+	+	+	+		+	+			+ (R)	Left
IV	22	+	Normal	?	Dullness	?	+	+					+		+ (R)		Left
V	29	?	Normal	?	Fine râles	?		+			+	+	+	+		+ (L)	Right
VI	19	+	37·7°–39°	+	None	+	+	+	+	+		+	+			+ (R)	Left
VII	49	+	37·5°–37·8°	+	None	+	+	+	+			+	+			+ (R)	Left
VIII	22	+	38°	+	None	+	+	+					+	+	+ (R)		Left
IX	27	+	37°–38°	+	None	+	+	+					+			+ (R)	Left
X	31	+	38°–40°	+	Bronchi	+	+	+	+				+	+		+ (R)	Left
XI	24	+	Normal	?	Dullness	+	+	+	+	+			+	+	None	None	Left
XII	14½	+	Normal	?	Moist râles	+	+	+			+	+	+		+ (L)		Right
XIII	29	+	37°–39°	+	None	+	+	+	+				+	+		+ (R)	Left
XIV	24	+	37°–40°	+	None	+	+	+	+				+		+ (R)		Left
XV	38	+	Normal	+	None	?		+			+	+	+		+ (L)		Right
XVI	30	+	Normal	+	Dullness	o	+	+					+			+ (R)	Left
XVII	14	+	38°–40°	+	Moist râles	+	+	+			+	+			None	None	Right
XVIII	32	+	39°	+	Dullness	+	+	+	+				+		+ (R)		Left
XIX	20	+	40°	+	None	o	+	+	+				+			+ (R)	Left
XX	17	+	Normal	?	?	?		+			+	+	+	+		+ (L)	Right
XXI	20	?	Normal	?	None	+	+	+	+	+			+		None	None	Left
XXII	23	+	38·4°	+	None	+		+	+				+	+	None	None	Left

* Interspace.

TABLE II

CLINICAL AND ROENTGENOLOGICAL FINDINGS IN 220 SELECTED CASES SHOWING CONTRALATERAL BRONCHIAL INFECTION

Symptoms
Sputum 213 (97%). Cough 211 (96%). Fever 160 (73%)
Abnormal physical signs in secondarily infected lungs
Dullness, breath sounds, râles, etc. 108 (49%). Râles 44 (20%).
Sputum
Tubercle bacilli present 99 (92%); absent 19 (8%); unknown 102.
Roentgenological findings
Cavity on original side 196 (89%).
Parenchymatous infiltration on contralateral side, from left to right lung 71 (32%), of which 69 (94%) in second interspace area; from right to left lung 149 (68%); of which 140 (94%) in third interspace area.

(6) That secondary bronchial cross infection in pulmonary tuberculosis is usually peripherally situated and involves the parenchyma of the lungs. The infectious material must therefore be aspirated into the air vesicles proper. Continued lying on the secondarily diseased side during sleep is apparently the main factor causing the drainage into the parenchyma of exudate which is present in the bronchi.

There is at least one important lesson to be learned from our study which has a practical bearing on the handling of patients with pulmonary tuberculosis. It is probable, as was shown in our experiments, that the passage of loose foreign matter from one lung to the other is largely controlled by gravity. Usually, during waking hours, excessive secretions leaving a cavity, or loose detritus and mucus from active tuberculous lesions will be more or less completely and immediately evacuated by cough and expectoration. Where, however, cough is controlled (by sedatives or by voluntary suppression) and when the cough reflex is more or less completely inhibited during sleep, immediate evacuation of material entering the bronchi does not occur. With the patient lying on his side, such secretions will pass by gravity from the uppermost lung and enter the bronchi of the dependent lung to be distributed to the area of predilection of that lung. With this understood, prevention of contralateral bronchial infection becomes a simple matter of posture. Patients with tuberculous lesions in one lung should always sleep on the affected side, and should spend as many as possible of their waking hours in this position. Other authors[3,4,5] have advised such postural rest for their patients, but do not include the prevention of contralateral infection among the reasons for giving such advice.

Another lesson of some value that we have learned is the importance of paying particular attention to the examination of the axillary area of the opposite lung where frank signs of disease are found on one side. In this region—one that is frequently missed in a hurried examination—the signs of early contralateral infection must be sought particularly in the absence of apical disease on the same side.

REPORTS OF ILLUSTRATIVE CASES

CASE I. M. C. L., male, aged twenty-four. January 27, 1930: Fever, loss of weight, cough with copious sputum, positive for tubercle bacilli. Right lung—dullness, prolonged expiration in upper. Roentgen examination (Fig. 8, *I*): Right lung—large cavity with fluid level in upper area. Left lung—clear. February 18, 1930: High continuous fever. Cough less. Dullness, amphoric breath sounds over the right upper lung. No abnormal physical findings in left lung. Sputum positive for tubercle bacilli. Roentgen examination (Fig. 8, *II*): Right lung—reduction in size of original large cavity; development of small cavities medial to large one. Left lung—new infiltration in anterior third interspace.

CASE II. T. H. L., female, aged fourteen. April 15, 1931: Fever, cough, mucopurulent sputum, positive for tubercle bacilli. Roentgen examination (Fig. 9, *I*): Left lung—active tuberculous infiltration in first and second interspace area. Suggestive small cavities. Right lung—clear. May 7, 1931: Persistent fever. Increase in dullness of left upper area. No abnormal physical findings in right lung. Roent-

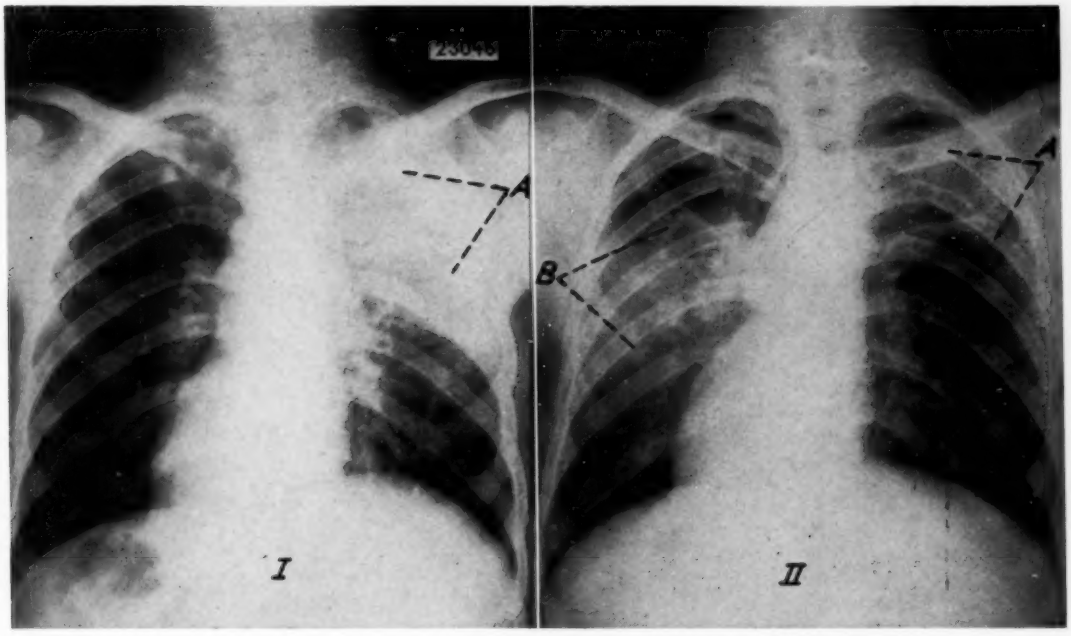

Fig. 8. Case I. First roentgenogram (*I*) taken January 27, 1930 and second (*II*) February 18, 1930.

gen examination (Fig. 9, *II*): Left lung—marked extension of lesion with multiple cavities. Right lung—definite minimal infiltration in second interspace area.

Case III. H. H. C., female, aged twenty-two. August 24, 1932: Fever, cough, sputum, dullness and râles in right upper lung. Roentgen examination (Fig. 10, *I*): Right lung—exudative lesion with cavity in upper area. Left lung—clear. November 23, 1932: Bed-rest. No cough. No fever. Sputum positive for tubercle bacilli. Roentgen examination: Right lung—improvement of lesion in upper area. Left lung—minimal infiltration in third interspace area. August 19, 1933: Continued bed-rest, no fever. Roentgen examination (Fig. 10, *II*): Right lung—slight extension of lesion in upper area, cavity larger. Left lung—soft parenchymal infiltration in third interspace area near periphery.

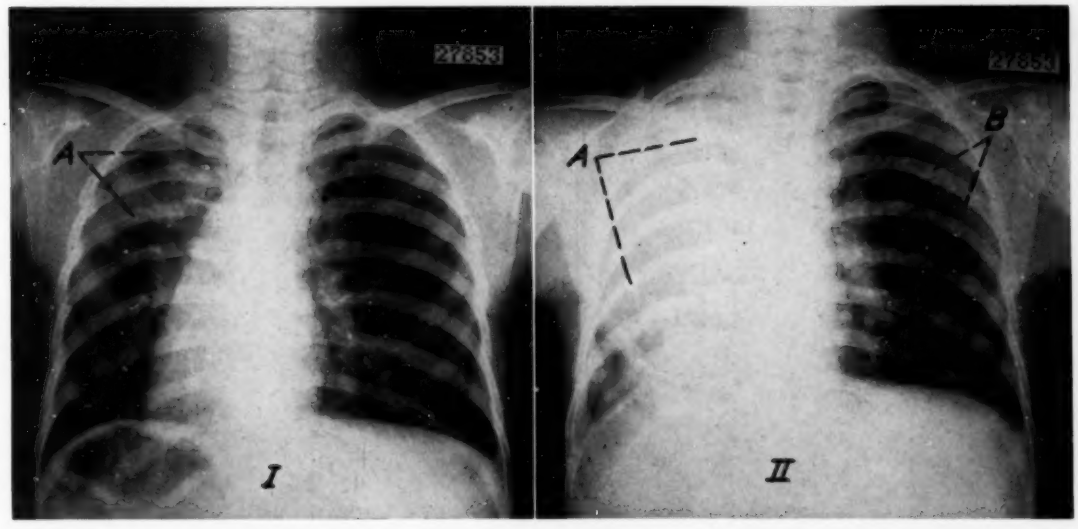

Fig. 9. Case II. First roentgenogram (*I*) taken April 15, 1931 and second (*II*) May 7, 1931.

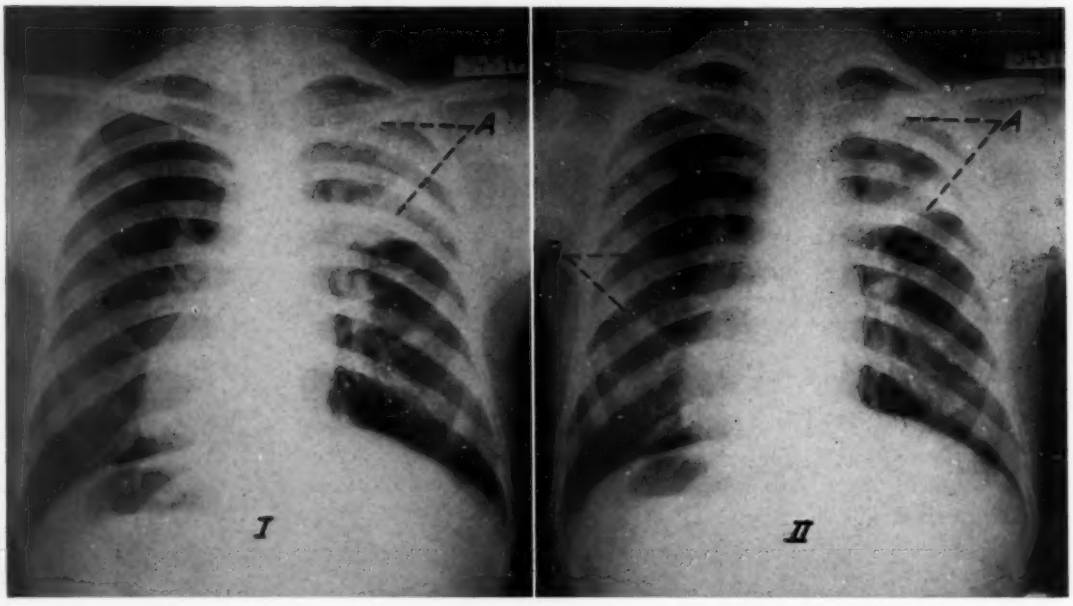

FIG. 10. Case III. First roentgenogram (*I*) taken August 24, 1932 and second (*II*) August 19, 1933.

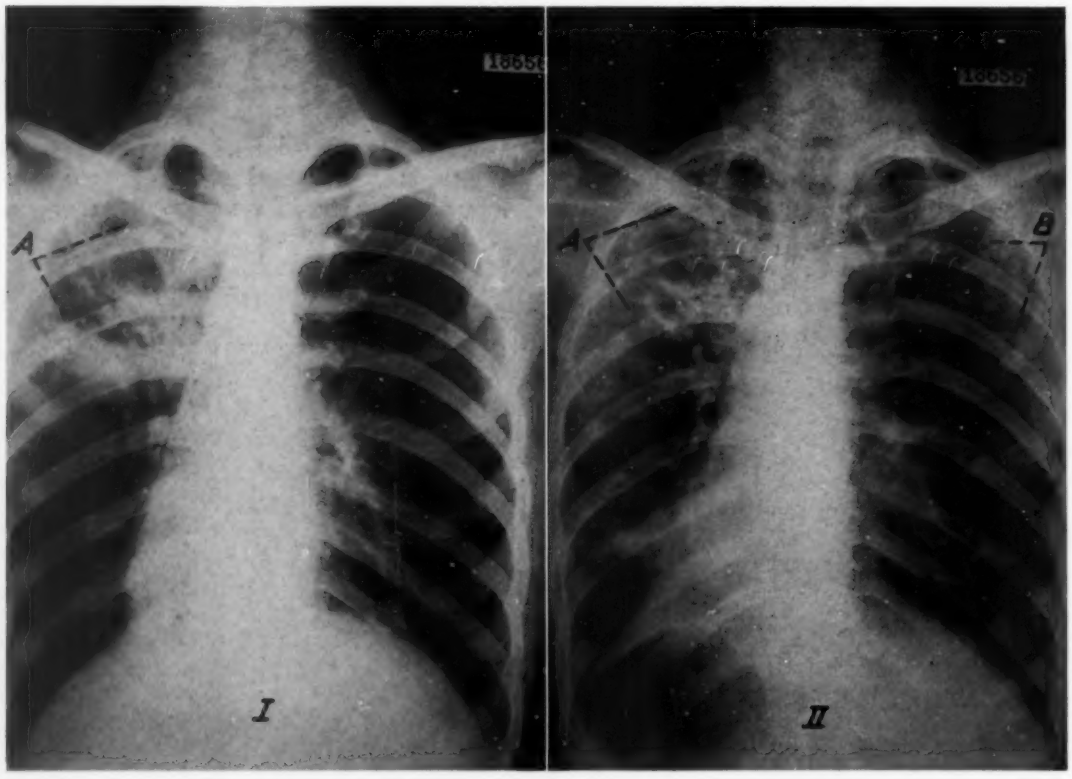

FIG. 11. Case IV. First roentgenogram (*I*) taken September 14, 1928 and second (*II*) August 26, 1929.

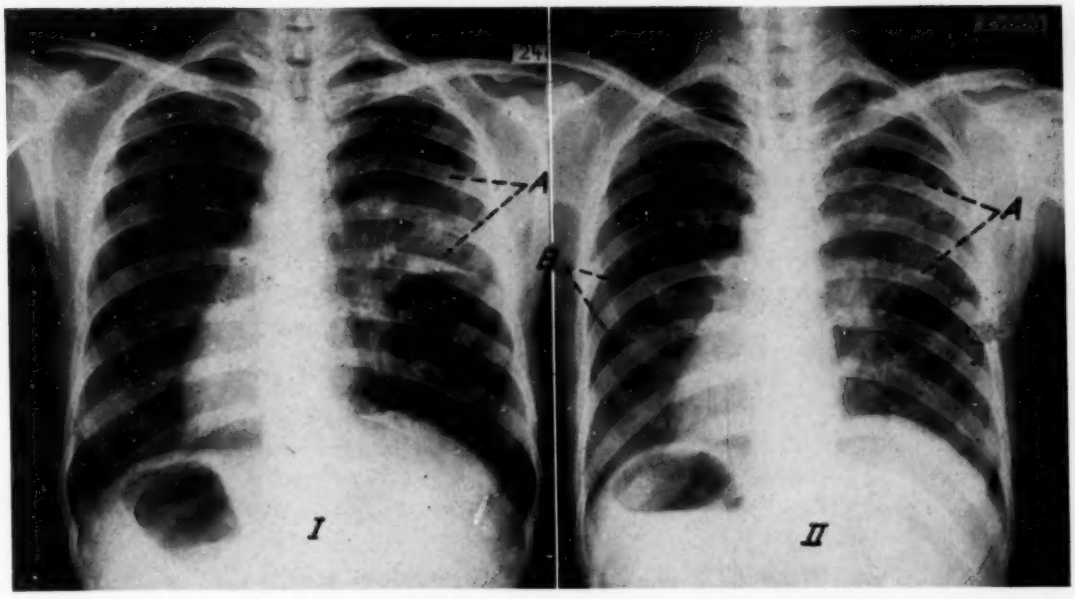

Fig. 12. Case v. First roentgenogram (*I*) taken June 30, 1930 and second (*II*) July 17, 1930.

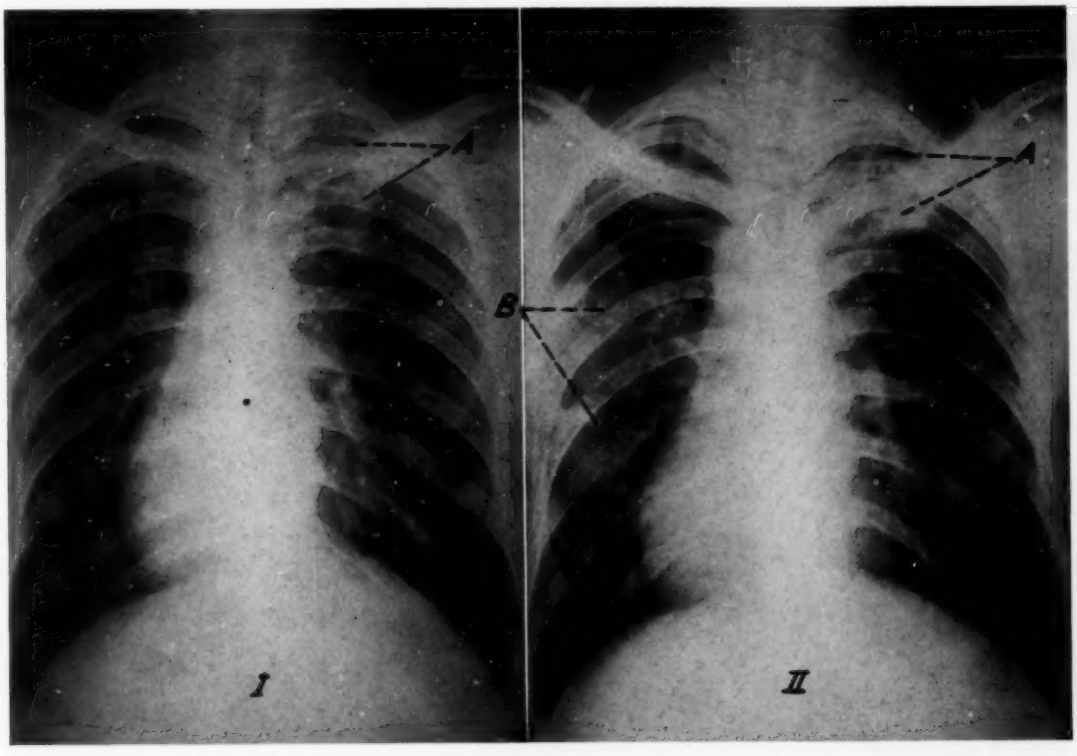

Fig. 13. Case vi. First roentgenogram (*I*) taken June 25, 1931 and second (*II*) September 7, 1933.

CASE IV. T. Y. P., male, aged twenty-three. September 14, 1928: Weakness, loss of weight, dry cough for three months. Dullness and râles in left upper lung. Sputum positive for tubercle bacilli. Roentgen examination (Fig. 11, *I*): Right lung—clear. Left lung—extensive lesion with large cavity. August 26, 1929: Bed-rest at home without improvement. Constant cough and sputum. Fine râles above right scapula. Dullness, suppressed breath sounds and medium râles in left upper lung. Roentgen examination (Fig. 11, *II*): Right lung—new mottled infiltration in second and first interspace area. Left lung—infiltration with multiple cavities apex to fourth interspace area.

CASE V. L. W. S., female, aged thirty. June 30, 1930: Afternoon fever, loss of weight, cough with blood-streaked sputum for ten days. Fine râles in right upper lung. Roentgen examination (Fig. 12, *I*): Left lung—clear. Right lung—extensive infiltration with multiple cavities. July 17, 1930: No improvement. Roentgen examination (Fig. 12, *II*): Left lung—definite parenchymal infiltration in third interspace near periphery. Right lung—about the same as before.

CASE VI. K. T. H., male, aged twenty-two. June 25, 1931: Sudden development of cough on June 22. Hemoptysis June 23 and 24. Dullness over right upper. Roentgen examination (Fig. 13, *I*): Right lung—active lesion in upper area. Left lung—clear. September 7, 1933: No treatment. Occasional streaking of sputum with blood during last six months. Dullness both upper areas. Roentgen examination (Fig. 13, *II*): Right lung—extension of the lesion with the development of a cavity. Left lung—new lesion in second and third interspace areas.

CASE VII. F. Y. T., male, aged thirty-one. January 27, 1930: Fever, night sweats, fatigue, cough and sputum for one month. Dullness and moist râles over right upper lung. Roentgen examination (Fig. 14, *I*): Left lung—scar in apex. Right lung—infiltration with cavitation in upper lobe. March 1, 1930: Cough and sputum less. Roentgen examination: Left lung—definite minimal new infiltration in third interspace area near periphery. Right lung—no change. June 23, 1930: Resting at home. Increase in cough and sputum. Dullness in both upper lungs. Râles in right upper and throughout left lung. Roentgen examination (Fig. 14, *II*): Left lung—marked extension with development of cavity in second and third interspace area. Right lung—clouding in upper area less than before.

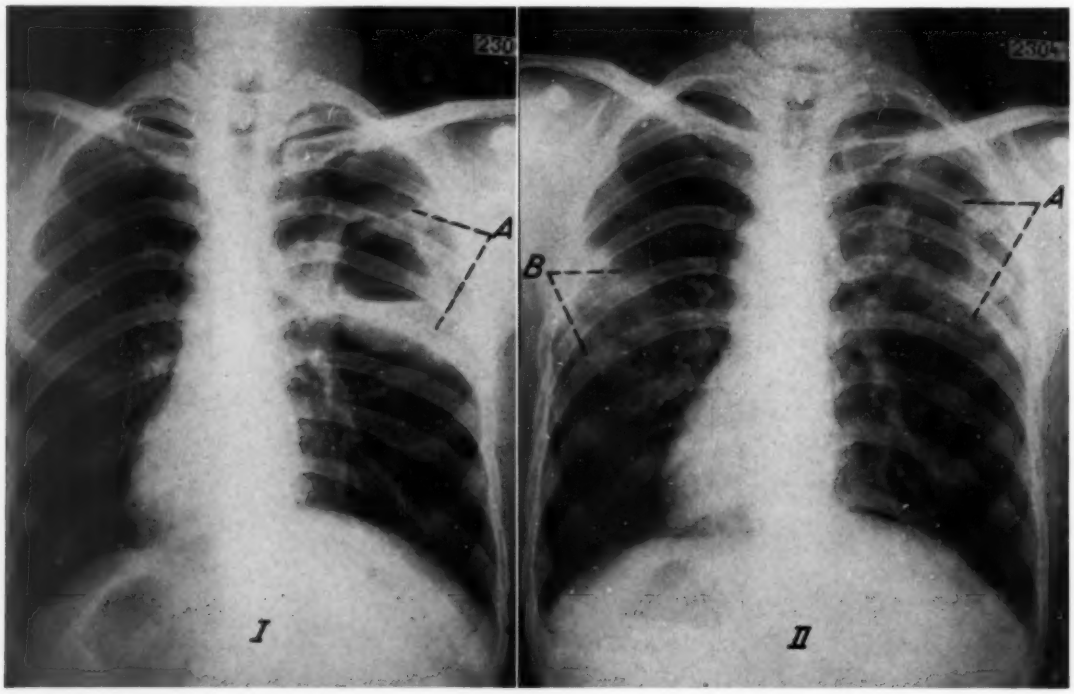

FIG. 14. Case VII. First roentgenogram (*I*) taken January 27, 1930 and second (*II*) June 23, 1930.

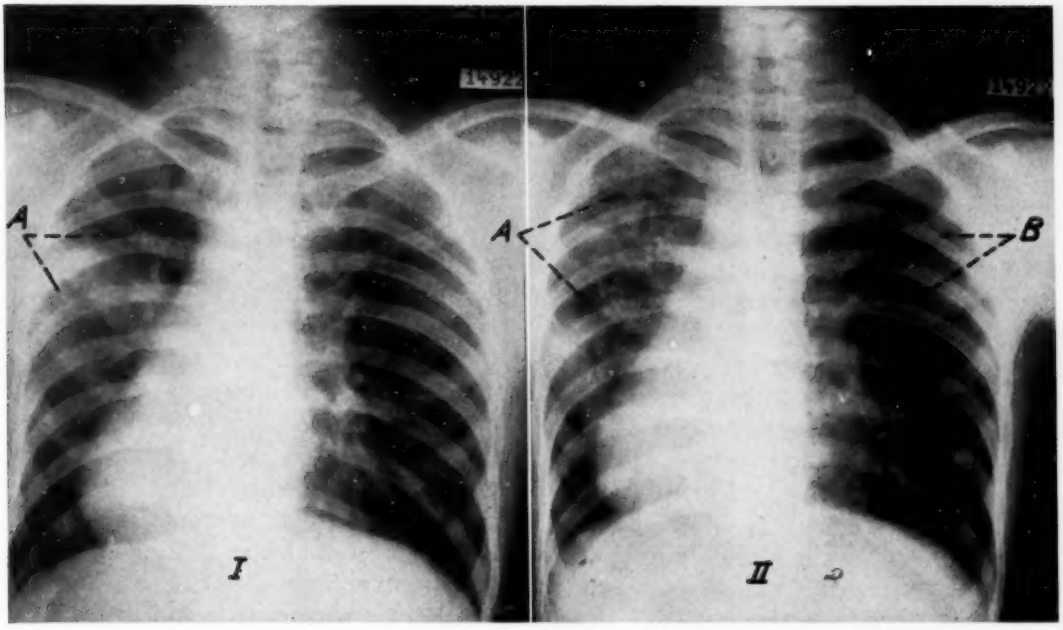

Fig. 15. Case viii. First roentgenogram (*I*) taken December 12, 1927 and second (*II*) December 6, 1928.

Case viii. H. C., male, aged seventeen. December 12, 1927: Cough and sputum for three years. Has had treatment in a sanatorium. Roentgen examination (Fig. 15, *I*): Right lung—clear. Left lung—infiltration in second interspace area. December 6, 1928: Bed-rest in sanatorium. Hemoptysis one week ago. Tubercle bacilli in sputum. No fever. Dullness and râles in left upper lung. No abnormal findings on right side. Roentgen examination (Fig. 15, *II*): Right lung—new infiltration in second interspace area. Left lung—marked extension of lesion.

SUMMARY AND CONCLUSIONS

1. Experiments are described which show that under the force of gravity and with cough controlled, fluids and oily suspensions will pass from one lung to reach the parenchyma of the opposite lung.

2. The findings in twenty-two cases of contralateral bronchial infection of lungs previously shown to be healthy are described.

3. Two hundred and twenty further cases of bilateral pulmonary tuberculosis which seem to show the phenomenon of contralateral bronchial infection are summarized.

4. Limited and well defined areas, differing in the two lungs, are found to be more liable to contralateral bronchial reinfection than the remainder of the lung field.

5. The area of predilection for the right lung is projected in routine posteroanterior roentgenograms as the second anterior interspace near the periphery; that for the left lung is the third anterior interspace.

6. Patients with unilateral pulmonary tuberculosis should sleep on the affected side.

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REGIONAL ILEITIS*

A REVIEW OF FIFTY CASES

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INTRODUCTION

IN 1932, Crohn, Ginzburg, and Oppenheimer[8] segregated from the various types of benign intestinal granulomata, a specific entity which they designated as regional ileitis. They described a granuloma of the terminal ileum characterized by a cicatrizing, inflammatory process which produced stenosis of the involved segment of intestine. Clinically the symptoms resembled ulcerative colitis in many instances, because diarrhea, abdominal pain, fever, and emaciation were often present. A mass was usually present in the right lower quadrant of the abdomen.

During the past three years there has been an active interest in the subject, which is made evident by the increasing number of cases reported in the literature. Since the publication of the original article in 1932, over 100 cases have been reported.

The diagnosis, even though it may be suspected clinically, depends primarily on the roentgen examination. The present study is a review of 50 cases of regional ileitis seen during the past three years at Mount Sinai Hospital, with particular reference to the roentgen findings.

When the original group of 14 cases was first studied by Crohn, Ginzburg, and Oppenheimer, the process was limited to the terminal ileum. Since then the greater number of cases available for study has somewhat modified the original conception of the disease. A similar pathological process has been noted, involving other parts of the intestine, for example, the proximal ileum and jejunum. In addition, cases of regional ileitis have been found to be associated with ulceration of the cecum and proximal colon. These cases of regional ileitis with colitis have been designated by Crohn as the "combined form" of the disease.

During the past three years 9 cases have been reported in the literature with a similar pathological process in which either the jejunum alone, or the jejunum and ileum were involved. In view of this, the term regional ileitis has been considered as not sufficiently comprehensive. "Chronic cicatrizing enteritis,"[14] "chronic ulcerative enteritis,"[6] and "regional enteritis,"[2] have been suggested as being more descriptive of the pathological process. The fact remains, however, that although the disease may affect various segments of the intestine, there is a definite predilection for the terminal ileum in a large majority of the cases, and in this respect the term regional ileitis is still appropriate. It might perhaps be advisable to classify the whole group in the true pathological sense as nonspecific ulcerative granulomas of the intestine, and reserve the name regional ileitis for those cases where the ileum alone is involved. By using the term "ulcerative" this group is differentiated from the other nonspecific granulomas of the intestine, such as occur following perforation of the bowel (e.g. fishbone) or those associated with diverticulitis of the colon, and so forth.

PATHOLOGY

The pathological changes associated with both the acute and chronic forms of the disease should be discussed. Most of the knowledge regarding the pathology of acute ileitis has been obtained from observations made in the operating room, on cases that were operated on with a preoperative diagnosis of acute appendicitis. In these instances the appendix either appeared normal or showed only microscopic evidence of chronic inflammation. The terminal ileum presented a characteristic picture. It was found to be thickened and

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edematous. The serosa was injected and had a red appearance. The mucosa of the bowel showed evidence of recent ulceration. The mesentery was thickened and contained numerous hyperplastic lymph nodes. Such cases have been reported by Clute,[5] DeCourcy,[9] and Jackman.[15] Reports of acute ileitis in children have been presented by Rockey,[18] and Erb and Farmer.[10] Felsen[12] has reported 5 cases of acute ileitis associated with the cultural and serological findings of bacillary dysentery.

The cases of chronic ileitis also have a very characteristic pathological picture. In most cases the process is limited to the terminal ileum. The lesions extend proximally for varying distances from the ileocecal valve, usually 10 to 15 inches of the intestine being involved. There is marked thickening and hypertrophy of the wall of the terminal ileum so that it may be two or three times the normal size. As a result of this process, there is marked stenosis of the lumen of the intestine. The narrowing is most marked in the region of the ileocecal valve and terminates abruptly at this point. Proximally, the condition lessens in severity, so that there is a gradual transition to normal bowel. The intestine proximal to the involved segment shows moderate dilatation as a result of the stenotic process in the diseased area.

In the proximal portions of the resected specimens, multiple oval and lenticular ulcers are present, usually on the mesenteric border of the bowel. These vary in size and are found proximal to the main hypertrophic mass, separated from it by strips of normal-appearing mucosa. Distally, the ulcers become confluent so that the entire mucous membrane is denuded except for a few islands of mucosa. In the more advanced cases, the mucosa is pale, alternately atrophic and hypertrophic, with evidence of diffuse scarring. The ridges and folds of mucous membrane associated with polypoid hyperplasia give the mucosa grossly a cobblestone appearance.

The submucosa is greatly thickened, contributing to the marked diminution in the caliber of the intestinal lumen. The serosa is often granular and occasionally tubercle-like structures are present on the surface. The mesentery of the intestine is thickened and contains many large hyperplastic lymph nodes.

In some of the cases, changes in the cecum and proximal colon are associated with the granuloma involving the terminal ileum. Pericecal fibrotic and inflammatory changes are often present which produce thickening and induration, resulting in deformity of the cecum. Internal fistulae between the cecum and the involved loop of ileum also contribute to these changes.

In addition to the above group, there are cases of regional ileitis associated with ulcerative colitis which show evidence of an ulcerative process involving the adjacent cecum and colon. The mucosa in these areas is congested, and irregular patches of ulceration are present. In some instances the ulcerations are limited to the cecum but more frequently there is involvement of the ascending colon. Rarely there has been evidence of a diffuse colitis involving almost the entire colon. The ulcerative process in the colon has been interpreted pathologically as a nonspecific ulcerative colitis associated with the primary granuloma of the terminal ileum, rather than an extension of the granuloma per se into the colon.

At times, the pathological picture is complicated by the formation of both internal and external fistulae, which result from the tendency of these granulomatous lesions to perforate. These fistulae communicate with the cecum and colon where the diseased ileum has become adherent. Walled-off abscesses in the mesentery and adjacent to the ileum are also encountered as a result of the tendency to perforation.

Microscopically, various stages of acute and chronic inflammation are present. In some cases the presence of foreign body giant cells results in the formation of tubercle-like structures which may simulate the anatomical tubercles of tuberculosis. However, smears, cultures, and guinea

pig inoculations for the demonstration of the tubercle bacillus have been repeatedly negative. In view of the similarity of the gross pathology, it is quite easy to understand why many of these cases were wrongly classified in the past as primary hyperplastic tuberculosis of the intestine.

CLASSIFICATION OF CASES

	Number of Cases	Per Cent
1. Regional ileitis	50 (total)	100
(a) Acute	3	6
(b) Chronic	37	74
2. Regional ileitis with colitis	5	10
Ulcerations limited to cecum	4	8
3. Jejuno-ileitis	1	2

CLINICAL FEATURES

Crohn, Ginzburg and Oppenheimer classified their cases of regional ileitis into four clinical groups:

1. Signs and symptoms of acute intra-abdominal inflammation (acute ileitis). These cases present themselves with the clinical picture of acute appendicitis from which it is impossible to differentiate them. At operation a red, thickened and edematous terminal ileum is found. The appendix, most often, is normal.

2. Symptoms of ulcerative enteritis. Clinically these cases simulate nonspecific ulcerative colitis, and characteristically present abdominal pain, diarrhea, fever, loss of weight, and anemia.

3. Stenotic phase. In this group the clinical picture of a small bowel intestinal obstruction is present. Abdominal pain, vomiting, distention and visible peristalsis are evident.

4. Persistent fistulae. This complication usually results following drainage of an intra-abdominal abscess, after being erroneously considered appendicular in origin. Internal fistulae between the diseased ileum and various parts of the colon also occur.

In the present series of 50 cases 34 were males, a ratio to females of 2 to 1. The age incidence is significant in that most of the cases were young adults. The average age for all the cases was twenty-four years, and only 16 per cent of the cases were over thirty-five years of age; the youngest patient was fourteen and the oldest fifty-four. In 2 separate instances the disease affected sisters.

The duration of illness in most cases ranged between several months and several years. In some instances the complaints were only of several weeks' duration. The most common symptoms were abdominal pain, diarrhea and loss of weight. Occasionally, the symptoms were minimal and characterized only by mild abdominal pain or diarrhea, even where the involvement of the bowel was extensive.

Abdominal pain was the most common complaint, being present in 36, or 72 per cent, of the cases. The pain was present in the lower abdomen, particularly the right lower quadrant, usually being intermittent and cramp-like in nature.

Diarrhea was present in 26, or 52 per cent, of the cases. In most cases it was not very severe and consisted of several loose stools a day. One-half of the cases with diarrhea showed the presence of blood in the stools, either grossly or microscopically, but usually in the latter form.

Vomiting was present in 14, or 28 per cent, of the cases, and was particularly noticed in those cases showing marked stenosis of the intestinal lumen.

Loss of weight was conspicious in 60 per cent of the cases, being present in 30 cases of the present series.

Fever was present in 19, or 38 per cent, of the cases. It was usually low grade and intermittent in type.

The most constant finding on physical examination is the presence of a palpable mass in the right lower quadrant of the abdomen. This was present in 29, or 58 per cent, of the cases. The mass is firm, several centimeters in diameter and often tender on palpation. The mass is composed of the markedly thickened terminal ileum and its mesentery, containing hyperplastic lymph nodes. At times the presence of adherent intestine and chronic walled-off abscesses

in the surrounding tissues are contributory factors. In some instances only the thickened cord-like terminal ileum is felt in the right lower quadrant of the abdomen.

Fistula formation is characteristic of the disease and, in the present series, was present in 18, or 36 per cent, of the cases. These fistulae are of two types, both internal and external abdominal types being present. They usually occur spontaneously; however, in some cases, they are postoperative. In these instances they have usually followed incision and drainage of abdominal abscesses, most often considered appendicular in origin. These fistulae defy closure until the diseased segment of small bowel has been resected. The internal fistulae usually communicate between the terminal ileum and various parts of the small and large bowel where the diseased ileum has been adherent. The cecum, ascending colon and sigmoid were the regions most frequently involved.

Laboratory examination showed the presence of a secondary anemia in a considerable number of the cases, being present in 42 per cent of the series. Bacteriological studies and stool cultures have failed to demonstrate any specific organism as the etiological cause of the disease.

The clinical course of these cases demands surgical intervention as medical treatment is futile. Unless operation is resorted to, the disease progresses and may result in intestinal obstruction or fistula formation. Operation consists of resecting the diseased segment of small intestine. This procedure is occasionally preceded by a preliminary short-circuit operation, such as ileotransverse or ileosigmoidostomy. Surgical removal of the diseased bowel usually effects a cure, as these intestinal granulomas are benign in nature. The occasional disappearance of intestinal granulomas following a short-circuit operation is well known to surgeons.

SUMMARY OF CLINICAL FINDINGS

Number of cases		50	
Age		14–54 (average 24)	
Sex	Males	34	(68%)
	Females	16	(32%)
Previous appendectomy		14	(28%)
Abdominal pain		36	(72%)
Diarrhea		26	(52%)
Blood in stools		13	(26%)
Vomiting		14	(28%)
Loss of weight		30	(60%)
Temperature		19	(38%)
Palpable mass		29	(58%)
First symptom	Diarrhea	17	(34%)
	Pain	33	(66%)
Anemia		21	(42%)
Fistulae		18	(36%)
	Internal	10	(20%)
	External	8	(16%)

ROENTGEN DIAGNOSIS

Method of Study of the Gastrointestinal Tract

Before discussing our detailed method of study of the small intestine it might be advisable to mention the approach to the study of pathological conditions of the small intestine. Experience has shown that unless these lesions are sought for carefully, they may be very easily overlooked. In fact, a review of our case histories reveals that a number of them had examinations of the gastrointestinal tract previous to their admission to the hospital. These were considered negative. Presumably, the examiner focused his attention primarily on the stomach and duodenal bulb and disregarded the rest of the intestinal tract. It is of the utmost importance that special attention be focused on the small bowel, particularly the terminal ileum. This fact is worthy of special and repeated emphasis.

It is not very practical to do complete studies of the small intestine on all cases referred for examination of the gastrointestinal tract; however, certain points in the patient's history suggest the advisability of these special studies. For example, cases of persistent diarrhea of indeterminate etiology where ulcerative colitis has been excluded, and so-called cases of "colitis" where the barium enema and sigmoidoscopic examinations are negative, should be included in this category. Patients who complain of abdominal cramps are regarded

Fig. 1. Regional ileitis: Arrows point to narrow terminal ileum. Deformity on the medial aspect of the cecum also present, due to pressure of the adjacent mass (barium meal, three hour examination).

as suspects, particularly when the patient has had a previous appendectomy. The indications, of course, are direct when physical examination reveals the presence of a mass in the right lower quadrant of the abdomen, or in cases that present themselves with persistent fecal fistulae following previous appendectomy. It is advisable to pay special attention to the terminal ileum on all routine six hour roentgenoscopic examinations, particularly in those cases where the stomach and duodenum show no abnormality.

In all suspected cases serial films are taken at frequent intervals following the ingestion of the barium meal. Usually they are taken at one, two, four, six and eight hours, p.c., and more frequently when indicated by the roentgenoscopic examination. All films are taken in the prone position. The barium meal is of course contraindicated whenever there is any clinical evidence of intestinal obstruction, either partial or complete.

Occasionally films are taken with the roentgen tube in place during roentgenoscopy. In this way the patient may be rotated and films taken in the particular position which will best demonstrate the lesion. All routine cases that show a delay in the motility of the small intestine at the six hour examination (no barium in the colon) have films taken at this time and return two hours later for re-examination. At this time the terminal ileum, cecum and part of the ascending colon are usually demonstrated.

The barium enema has been found to be of distinct value. A definite attempt is made to fill the terminal ileum in most cases referred for examination of the colon. In this way, occasional cases will be found which might otherwise be overlooked. It is used in all cases of terminal ileitis, particularly in those cases that show evidence by the barium meal of cecal or colonic involvement. In this way the findings in the proximal colon are confirmed when these regions are involved, and the extent and type of pathology are accurately determined.

Roentgen Findings

The roentgen changes in nonspecific ulcerating granulomas will be considered under the following headings: (1) regional ileitis; (2) cecal deformity associated with regional ileitis; (3) regional ileitis with colitis; (4) nonspecific jejuno-ileitis; (5) fistulae.

(1) *Regional Ileitis.* In regional ileitis the essential roentgen finding is the demonstration of a cicatrized and stenosed terminal ileum. The normal caliber of the terminal ileum is reduced to one-half or one-third of its normal size, and is represented by a thin stream of barium leading to the cecum. The narrow tract may be shown extending various distances from the cecum, and at times the process may be demonstrated as involving up to 8 or 10 inches of the terminal ileum, more often 5 or 6 inches (Figs. 1 and 2).

Usually the narrowing of the terminal ileum is irregular, some parts being more involved than others. The margins of the

involved ileum are usually smooth and there is obliteration of the normal mucosal markings. In rare instances small, round transparencies within the barium-filled viscus may be observed, representing a polypoid appearance in the mucosa of the bowel. The process ends abruptly at the ileocecal valve.

The narrow terminal ileum is best demonstrated by the barium meal at the four, six, and eight hour observations. The changes found in the bowel are constant during the entire examination, even on re-examination at a later date. The normal variation in the appearance of the terminal ileum must be kept in mind. Occasionally a normal terminal ileum appears narrowed, due to spasm or incomplete filling. These changes, however, are not constantly present, when observations are made later during the examination or at a later date.

In some instances the ulcerations in the mucosa of the diseased bowel result in irritability of the involved segment so that it does not retain any barium. In these cases the terminal ileum is never satisfactorily demonstrated at any time during the examination (Figs. 3 and 5). At times a normal terminal ileum will not be visualized and should not be confused with the above findings, for in these cases the changes are not constant.

When one considers the pathology of regional ileitis, one would expect constant dilatation of the intestine, proximal to the diseased segment. This, however, is not always demonstrated roentgenologically. In fact, it does not usually occur until the stenosis is quite marked.

In a large number of cases, a mass is present in the right lower quadrant of the abdomen. In these cases displacement of the normal loops of small bowel by the mass is very often demonstrated.

(2) *Cecal Deformity Associated with Regional Ileitis.* Occasionally, deformities of the cecum are to be noted (Figs. 1 and 2). In some cases there will be deformity of the cecal tip due to spasm. These changes, however, are not persistent, and if present with the barium meal, a complete cecum can usually be demonstrated by barium enema. More often there is a smooth semilunar defect on the medial aspect of the cecum due to pressure from the adjacent ileal mass. In some instances, changes in the cecum are due to adhesions in the region of the granuloma. In addition, fistulae and chronic walled-off abscesses, adjacent to the cecum, also produce deformity of this viscus. When these are present the cecum is very often constricted and irregular in outline. There is no mucosal ulceration of the cecum in this group, and Stierlin's sign is not present. This is significant and is of use in differentiating this group from the combined form of ileitis and colitis where mucosal ulceration plays a prominent part. To recapitulate, the essential roentgen findings are as follows:

1. Stenosis of the terminal ileum.
2. Constant non-visualization of the involved segment in some cases.
3. Dilatation of the intestine proximal to the involved segment.
4. Deformity of the cecum.

Fig. 2. Narrow terminal ileum demonstrated by barium enema. Note the cecal deformity due to pressure and adhesions from the adjacent mass.

Fig. 3. Regional ileitis associated with proximal colitis. Arrows indicate the narrow terminal ileum with segmented appendix in situ.

5. Displacement of the normal intestine by a mass in the right lower quadrant when present.

(3) *Regional Ileitis with Colitis.* In the combined form of ileitis and colitis the ulcerations may be localized to the cecum or involve the entire colon. Most often the cecum and proximal colon are involved (Fig. 3). One case in the present group developed evidence of a diffuse ulcerative colitis several years following the resection of the primary granuloma of the ileum, at which time the colon was found to be normal. In addition, this patient also has a recurrence of the original process found in the ileum (Fig. 4).

With the combined form of ileitis and colitis, the following roentgen changes are noted: Stierlin's sign is almost always present. The cecum and proximal colon show marginal irregularity and often appear contracted. The ulcerative process is manifested roentgenologically by spasm, irritability, and localized hypermotility of the involved segment of bowel, so that it retains very little barium either by barium meal or enema. The presence of these findings differentiate this group from the previous one where there is cecal deformity but no evidence of mucosal ulceration. It is worthy of note that the roentgen findings in these combined cases of ileitis and colitis resemble those which have been suggested by many as characteristic of ileocecal tuberculosis. This is exactly what one would expect in view of the similarity of the gross pathology in the two conditions.

(4) *Nonspecific Jejuno-ileitis.* Regional ileitis involving the proximal part of the small intestine is uncommon. Two cases are included in this group. In one, the involved segment was in the middle of the ileum, the terminal ileum showing no evidence of disease. The other case showed extensive involvement of both jejunum and proximal ileum in addition to the characteristic findings of regional ileitis in the terminal ileum. A third case of jejuno-ileitis previously reported by Schapiro[19] has been excluded from the present series. The pathological findings in this case were suggestive of tuberculosis because of the

Fig. 4. Recurrent lesion in terminal ileum associated with diffuse ulcerative colitis which occurred after the initial resection of the diseased ileum (barium meal, seven-hour examination).

presence of numerous typical anatomical tubercles in the adjacent lymph nodes; however, it was not possible to demonstrate the tubercle bacillus either by direct examination or guinea pig inoculation. The gross pathology in this case was almost identical with that seen in regional ileitis.

In our own case, the jejunum was involved for at least 12 inches. The lumen was irregularly narrowed, and the normal mucosal pattern was replaced by many oval and round transparent areas which were suggestive of polypoid excrescences in the mucous membrane. In addition, the terminal ileum appeared stenotic and presented the characteristic picture seen in regional ileitis (Fig. 5).

(5) *Fistulae.* Cases presenting themselves with external abdominal fistulae are first given indigo carmine by mouth to note if the tract communicates with the lumen of the intestine. Following this, the sinus tract is injected with lipiodol, under roentgenoscopic control, in order to note its extent, direction, and intestinal communication if possible. Internal fistulae are very difficult to demonstrate by barium meal or enema. When present, narrow sinus tracts are shown communicating with the involved portions of bowel (Fig. 6).

Fig. 5. Jejuno-ileitis: Upper arrows indicate an extensive lesion in the jejunum. Lower arrows point to terminal ileum which is narrow and retains very little barium (barium meal, four-hour examination).

Fig. 6. Fistulous communication between the ileum and proximal transverse colon where the diseased ileum has become adherent (barium enema, post-evacuation examination).

We have seen 2 cases where a primary lesion of the sigmoid was suspected because of the presence of an ileosigmoidal fistula. Operation demonstrated the presence of a primary granuloma of the terminal ileum with a sigmoidal fistula. The presence of ileosigmoidal fistulae in young adults should lead one to suspect a primary granuloma of the ileum rather than malignancy of the sigmoid, which is the usual condition in older adults.

Discussion of the Roentgen Aspects. The roentgen findings in regional ileitis are characteristic of the disease. However, as Kantor has pointed out, the changes are characteristic but not pathognomonic, as they may occur in other stenosing lesions of the terminal ileum. These instances are rare so that the correct roentgen diagnosis can usually be made with very little reservation. In the combined form of ileitis and colitis, interpretation is more difficult. Vari-

ous ulcerative diseases that involve the ileocecal region may give a very similar roentgen picture, and differentiation is not always possible.

DIFFERENTIAL DIAGNOSIS

In a consideration of the differential diagnosis special attention must be given to two diseases: namely, "primary" hyperplastic ileocecal tuberculosis, and nonspecific ulcerative colitis limited to the proximal colon with involvement of the terminal ileum. Both of these diseases may resemble regional ileitis very closely, particularly the "combined form" of the disease. The similarity occurs not only clinically but pathologically and roentgenologically.

Other specific granulomas which may involve the intestine must also be considered. Hodgkin's disease, lymphosarcoma, actinomycosis, and the amebic granulomas are mentioned. Malignant tumors of the proximal colon must be kept in mind. The various other nonspecific granulomata of the bowel should be excluded. In this category we can place the granulomas associated with diverticulitis or those that follow perforation of the bowel by a foreign body. In order to differentiate all these various processes, it is of the utmost importance not to rely on the roentgen examination alone. The history, physical examination, and the laboratory findings, are essential in arriving at a proper diagnosis.

1. *Tuberculosis.* Ulcerative intestinal tuberculosis occurring secondary to a pulmonary lesion is well known and is found quite frequently in patients with active pulmonary tuberculosis. The hyperplastic type is not as common as the former and may occur with or without associated pulmonary lesions. Most of the cases of this type reported in the literature have had a coexisting tuberculous process in the lungs. Rockey[18] states that there were only 9 cases of hyperplastic tuberculosis of the terminal ileum reported in the literature up to 1933. So-called "primary" hyperplastic ileocecal tuberculosis, in which the disease is limited to the intestine alone, and without evidence of tuberculosis elsewhere in the body, is very rare.

Moschowitz and Wilensky,[17] in 1923, pointed out the similarity in pathology between nonspecific granulomas of the intestine and "primary" hyperplastic intestinal tuberculosis, and stated that "many if not the majority of the so-called hyperplastic tuberculosis of the colon are really simple granulomata." Study of the pathological material in the present cases seems to substantiate their statement. Many of our cases have shown a pathological picture, both gross and microscopic, that simulates hyperplastic tuberculosis very closely.

Review of the literature on primary hyperplastic intestinal tuberculosis reveals the fact that in many of these cases tubercle bacilli were not demonstrated, the diagnosis in most instances being based on the presence of tubercles. When we consider that foreign body giant cell tubercles are present at times in these intestinal granulomas, the diagnosis in some of these cases of primary hyperplastic tuberculosis may be questioned. The demonstration of the tubercle bacillus is of prime importance in the diagnosis in these cases.

In a previous communication from this Hospital, when regional ileitis was not recognized as an entity, 3 cases of hyperplastic intestinal tuberculosis were reported.[13] Two of these had associated tuberculous lesions in the lungs, whereas the third case, which showed no evidence of tuberculosis in the lungs was operated on, and pathological examination of the specimen failed to reveal any evidence of tuberculosis. This case proved to be one of the first cases of regional ileitis seen at this Hospital. The corrected diagnosis with comment was subsequently published by the authors.[13]

In 1911, Stierlin[20] first pointed out the absence of a normal barium shadow in the proximal colon in cases of ileocecal tuberculosis. Since then Stierlin's sign has at times been erroneously considered as characteristic of intestinal tuberculosis. Both Assmann[1] and Carman[4] have stated that Stierlin's sign may occur with any ulcerat-

ing lesion of the ileocecal region, and consequently, it should not be considered indicative of tuberculosis. Ileocecal tuberculosis, proximal colitis (specific and nonspecific), and ulcerating granulomas of the ileocecal region may all have a very similar roentgen appearance. The roentgen changes described by Brown and Sampson,[3] and others, as characteristic of intestinal tuberculosis, have all been found in cases with associated pulmonary lesions; consequently, one can readily realize the hazard of making a roentgen diagnosis of ileocecal tuberculosis on the basis of Stierlin's sign alone, especially when there is no evidence of tuberculosis in the lungs. In regard to "primary" hyperplastic ileocecal tuberculosis, the only method of exclusion is the fact that we have found it to be extremely uncommon when compared with regional ileitis. At Mount Sinai Hospital, during the past three years, there has not been a single case of the former that was proved pathologically. This is in direct contrast with the large number of cases of regional ileitis that were observed during the same period.

2. *Ulcerative Colitis.* Cases of regional ulcerative colitis where the process is limited to the proximal colon with involvement of the terminal ileum offer difficulty in diagnosis at times. The differentiation from regional ileitis with proximal colitis is not always clear cut. The problem is of definite importance when we consider that the treatment of ulcerative colitis is usually regarded as primarily a medical problem, whereas the treatment in these cases of regional ileitis is considered surgical. On a clinical basis differentiation is very difficult and at times impossible. In the localized form of proximal colitis, the sigmoidoscopic examination is usually negative, as the distal colon and rectum are not diseased. Except for its localization, the roentgen appearance of proximal colitis is identical with the generalized form. In the cases of proximal ulcerative colitis, where the terminal ileum shows evidence of ulceration without stenosis, the differentiation from regional ileitis with colitis can be made with some degree of assurance, because whenever regional ileitis is associated with colitis, the process in the terminal ileum is usually far advanced and shows evidence of considerable stenosis. We have learned from experience that the converse does not always hold, and the roentgen evidence of what appears to be a stenotic ileum does not exclude proximal colitis with involvement of the terminal ileum. We have seen 2 cases of proximal ulcerative colitis, where the involved terminal ileum had a roentgen appearance not unlike that seen in regional ileitis. In both cases the differentiation from the "combined form" of regional ileitis could not be made either clinically or roentgenologically; these cases are the exception to the rule. In summation, we can only conclude that differentiation of the two conditions is possible in most instances, whereas in other cases, it is impossible both clinically and roentgenologically.

Specific ulcerative colitis due to chronic bacillary dysentery cannot be differentiated from the nonspecific type clinically, or roentgenologically. The diagnosis depends on the recovery of the specific organism from the stools or a positive serum agglutination reaction.

3. *Specific Granulomas.* Lymphoblastoma. Hodgkin's disease and lymphosarcoma occasionally affect the intestine and may involve any part of the bowel. At times there will be clinical evidence of a generalized disease with enlargement of the superficial lymph nodes or mediastinal tumor. The diagnosis usually rests on the microscopic examination of an excised lymph node. Primary Hodgkin's disease of the small intestine is very uncommon. In a recent case in which the jejunum alone was involved, the process was characterized roentgenologically by irregular areas of constriction and dilatation of the diseased bowel.

Amebiasis. Amebic colitis is most commonly found in the cecum and proximal colon, with involvement of the terminal ileum in rare instances. Chronic cases may result in the formation of a granuloma in

the involved portion of the bowel. In these cases the diagnosis is based on the presence of *Endamoeba histolytica* in the stools. The disappearance of these granulomas with specific therapy has been noted in some cases.

Actinomycosis. This disease should always be considered in every case with a persistent abdominal fistula. The abdominal form usually originates in the cecum and very often results in the formation of a mass in the right lower quadrant. The diagnosis is based on the presence of the characteristic yellow "sulphur granules" in the discharge.

Malignant Disease. Occasionally carcinoma of the colon may offer difficulty in diagnosis. In these cases the age incidence is much higher than in regional ileitis. We have seen one case of carcinoma of the cecum with involvement of the terminal ileum where the roentgen appearance was very similar to that seen in regional ileitis. The patient was sixty years of age. At operation metastatic nodules were present in the liver.

CONCLUSIONS

A great deal has been learned about regional ileitis since its introduction as an entity three years ago; however, there is still much that is not known about the disease, and further investigation is desirable. As yet the etiology is unknown. There is no explanation of why young adults are characteristically afflicted. The relation of the disease to nonspecific ulcerative colitis, particularly proximal colitis, is yet to be determined. Felsen[11] contends that bacillary dysentery, distal ileitis, and nonspecific ulcerative colitis are merely different stages or manifestations of the same disease. The knowledge of acute ileitis is incomplete. Prolonged follow-up on these cases is indicated if the end-results are to be known, particularly in those cases that have not had surgical resection. Complete bacteriological studies on cases of acute ileitis might help to solve the question of etiology, as studies on the chronic cases have failed to shed any light on the subject. The follow-up on the cases of acute ileitis in children that have been reported in the literature will be of real value. The advisability of roentgen studies of the small intestine in children who complain of chronic intermittent abdominal distress is suggested, as the history in some of the chronic ileitis cases dates back a number of years often with very mild symptoms, and the disease may go unrecognized unless it is suspected and special studies made of the small intestine.

SUMMARY

(1) A review of fifty cases of regional ileitis is presented with particular reference to the roentgen findings.

(2) Pathologically, the disease is characterized by a cicatrizing inflammatory process which results in marked stenosis of the intestinal lumen.

(3) There is a definite predilection for the terminal ileum, although other parts of the intestine may be involved.

(4) The most frequent symptoms are abdominal pain, diarrhea, and loss of weight.

(5) The presence of a palpable mass in the right lower quadrant of the abdomen is the most constant finding on physical examination.

(6) The cases are segregated into the following types:

1. Regional ileitis.
   (a) Acute
   (b) Chronic
2. Regional ileitis with ulcerative colitis.
3. Regional ileitis with fistulae.
4. Jejuno-ileitis.

(7) The roentgen findings are as follows:

1. Stenosis of the terminal ileum.
2. Non-visualization of the involved segment in some cases.
3. Dilatation of the intestine proximal to the involved segment.
4. Deformity of the cecum.
5. Displacement of the normal small bowel by a mass in the right lower quadrant.

6. Presence of fistulae.
7. Evidence of associated colitis in some cases, with spasm, irritability, and localized hypermotility of the involved segment of bowel (i.e., Stierlin's sign).

(8) The resemblance to other diseases that affect the ileocecal region is mentioned, particularly tuberculosis, and proximal ulcerative colitis with involvement of the ileum.

(9) The designation of the disease as a "nonspecific ulcerative granuloma of the intestine" is suggested, the term "regional ileitis" being reserved for those cases where the ileum alone is involved.

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TRAUMATIC SEPARATION OF THE LOWER EPIPHYSIS OF THE RADIUS

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THE first reference to separation of epiphyses is found in the writings of Hippocrates. This is, however, of historical interest only, as he appears to have dealt with the subject briefly and with a great deal of uncertainty.

While the possibility of epiphyseal separation has been admitted by medical writers since earliest times it was not until the latter half of the nineteenth century that it began to be distinguished from true fracture.

Poland in his excellent book, "Traumatic Separation of the Epiphyses," has reviewed all previously reported cases that he felt were authentic and added to these his personal observations on clinical material and museum specimens. This work covers the subject very thoroughly up to 1898, yet only 112 cases of epiphyseal separation of the lower end of the radius are recorded. Eighteen of these showed arrest of growth with deformity.

Many of the early observations were based upon compound epiphyseal separations and necropsy material obtained from children dying from concurrent injuries.

With the advent of the roentgen ray, an ideal method was offered for the study of these injuries. With its aid the diagnosis is frequently made and with a high degree of accuracy.

Despite these facts, separation of the lower epiphysis of the radius has received but scant attention in recent years. The majority of the textbooks on surgery devote but a paragraph or two to the topic and mention the possibility of shortening. Fonteneau, Helmann, Bonta, Meténier and Zwicke have written their theses for the doctor's degree upon this subject and while all are excellent monographs none of them is available in English and in no instance have they followed a series of cases for any considerable period of time.

Several isolated instances of shortening of the radius have been reported (Table 1). However, the majority of the authors reporting these cases did not attend the patient at the time of the original injury, but have presumed that an arrest of growth occurred following separation of the lower radial epiphysis. It is entirely possible that some of the cases reported before the use of the roentgen ray may have been mild types of Madelung's deformity such as the one shown in Figure 1. This patient, a woman fifty years old, at the age of eleven fell on her right wrist. The injury was thought to be trivial at the time and no treatment was given. One or two years later deformity was first noticed which slowly increased. The wrist at the present time shows shortening of the radius, volar displacement of the wrist and undue prominence of the ulna posteriorly. In this particular instance the clinical diagnosis of arrest of growth following epiphyseal injury was entertained until the roentgenograms definitely showed it to be a Madelung's deformity.

TABLE I

Author	Year	No. Cases
Poland	1898	18
Walther	1905	1
Stimson	1905	2
Chaput	1907	1
Waechter	1908	1
Phemister	1914	1
Tanton	1915	1
Pilcher	1917	1
Smith	1922	1
Smith	1924	1
Watson	1932	2
McFarland	1932	1
Beekman	1934	1
Key and Conwell	1934	1

Reported isolated cases of shortening of the radius presumably due to arrest of growth following separation of the lower epiphysis. Poland's 18 cases were collected from the literature.

While everyone admits the possibility of an arrest of growth following an injury to the lower epiphysis of the radius, there have been but few series of patients followed either clinically or roentgenographically to determine the probability of occurrence of this deformity. The only reported groups including the present series are listed in Table II.

TABLE II

Author	Cases	Deformities
De Paoli	17	None
Goyrand	3	None
Hutchinson, Jr.	6	1
Poland	5	None
Peters	11	1
Massart and Cabouat	44	6
Smith	12	5
Gillies	30	5

Reported groups of patients followed over varying periods of time to determine end-result subsequent to separation of the lower epiphysis of the radius.

The present series of epiphyseal separations of the lower end of the radius consists of 35 such injuries occurring in 30 patients. (In 5 the lesion was bilateral.) All were examined roentgenographically both at the time of the original injury and again at a later period. The interval between the two examinations varied from six months to eight years, three months, the average time between the two examinations being three years, six months.

Twenty-two additional separations (total 57) were studied roentgenographically at the time of the original injury but no follow-up examination could be obtained in these patients.

ANATOMY

The center of ossification for the lower end of the radius normally, according to Shelton, appears at the age of six to eight months and fuses to the diaphysis around the eighteenth to nineteenth year, there being some normal variation. It has long been known that fusion usually occurs somewhat earlier in girls than in boys. With disease or injury there may be retardation of growth or premature fusion.

The ossified center of the epiphysis is composed of cancellous bone surrounded by a thin dense cortex and is separated from the diaphysis by the epiphyseal or conjugal cartilage which becomes narrower as the child grows older. Bone growth, in length, takes place at the junction of the diaphysis with the epiphyseal cartilage by the proliferation and successive ossification of cartilage cells. This area of most recent calcification, as might be expected, is the point of least resistance to injury.

FIG. 1. Madelung's deformity which clinically in mild cases may be confused with traumatic arrest of epiphyseal growth.

The periosteum, although rather loosely attached to the shaft, is very firmly adherent to the epiphysis. Numerous small blood vessels go directly to the epiphysis from the periosteum. Only a few small vessels extend into the epiphysis from the diaphysis.

INCIDENCE

In a series of 260 consecutive bone injuries in the region of the wrist before the closure of the epiphyses, separation of the lower epiphysis of the radius was present 57 times, an incidence of 22 per cent (Gillies). These findings are in accord with those of Carter whose series of 82 cases showed a 24 per cent incidence of epiphyseal injury.

ETIOLOGY

Of the 35 epiphyseal separations in this series the causative trauma was very definitely of two types: (1) those due to a fall,

FIG. 2. Typical separation of the lower epiphysis of the radius. Note the characteristic wedge-shaped fragment detached from the posterior cortex of the diaphysis.

usually from a considerable height, on the outstretched forearm and hand striking the ground in dorsiflexion; (2) those due to automobile backfire injuries.

AGE INCIDENCE

The ages of the patients varied from seven years, three months, to eighteen years, seven months, the average age being twelve years, ten months. Obviously those due to automobile backfire injuries were in older persons. There were seven in this group with an average age of sixteen years, five months. If this group is subtracted from the total (automobile cranking eventually will be eliminated due to increasing use of self-starters for motor cars), the average age is then reduced to eleven years, nine months, which even at the present time is a more representative figure.

PHYSICAL FINDINGS

Clinically the physical findings closely resemble those of fracture. There is always "wincing" tenderness corresponding to the site of the epiphyseal line. This area of tenderness is closer to the wrist joint in epiphyseal separation than in true fracture. Fracture of the lower radius before the closure of the epiphysis occurs almost always three-fourths of an inch or more above the wrist.

Displacement, if present, is nearly always posterior producing varying degrees of "silver fork" deformity which again, because of the close proximity of the epiphysis to the wrist, produces a sharper curve than is seen in most fractures. The ventral surface of the wrist is unduly prominent from the swelling which is constantly present and due to the prominence of the diaphysis.

A soft "cartilaginous" crepitus may at times be elicited but if not at once apparent undue force should not be used to determine its presence.

ROENTGENOGRAPHIC FINDINGS

The displacement roentgenographically varies from a mere loosening of the epiphysis to complete posterior displacement. Anterior displacement is so rare as to be a surgical curiosity. In each of 57 injuries observed roentgenographically there was a small wedge-shaped fragment detached from the posterior cortex of the diaphysis which remained attached to the epiphysis (Fig. 2). It is doubtful if separation ever occurs without this accompanying fracture of the diaphysis. This small fragment should always be looked for in roentgenograms of suspected epiphyseal separations of the lower end of the radius as it may be present and plainly visible on films in which no displacement of the epiphysis is apparent, yet it is impossible to conceive of this fracture being produced without a solution of continuity along the epiphyseal line.

While roentgenograms in the postero-anterior and lateral views should always be made in suspected cases, the lateral is by all means the more important as it best shows the small characteristic posterior fragment and reveals the amount of displacement or tilting present. The postero-anterior view often shows but little even though considerable deformity may be present. It is indispensable, however, in determining the presence of accompanying fractures of the ulna and the rare longitudinal fracture of the epiphysis itself.

PATHOLOGY

As pointed out by Ollier and Broca in typical so-called epiphyseal separations, the separation actually takes place between the diaphysis and the epiphyseal cartilage and not through the epiphyseal cartilage itself. Ollier therefore suggested the term "diaphyseal separation" (décollement diaphysaire). For similar reasons Rollet uses the term "juxta-epiphyseal separation." Others have favored calling these injuries fractures of the epiphyses. However, the term epiphyseal separation has been in general usage so long that it seems inadvisable to attempt to change the terminology at this late date.

But 2 cases out of 57 in this group were compound and only one was examined post mortem (the only case terminating fatally). This was that of a child aged ten dying from gas gangrene following a compound epiphyseal separation of the right radius. The findings were in accord with those of the elder Hutchinson published in 1862. His description is so excellent that I cannot refrain from quoting it verbatim. Hutchinson's patient was a boy of sixteen who died a few days after admission to the hospital from various severe injuries sustained in a fall. His description is as follows:

> The specimen shows complete detachment of the carpal extremity (epiphysis) of the radius. The detached fragment bears its normal relations with the carpal bones, none of the ligaments having been injured. The line of separation (proximal aspect of the epiphysis) is everywhere covered with cartilage, excepting that, on its dorsal aspect on the inner side, a small portion of bone has been broken from the extremity of the shaft, and carried along with the epiphysis. The lower extremity of the shaft presents no cartilaginous covering, but shows numerous rounded elevations which had fitted into corresponding depressions in the cartilage of the epiphysis. Its surface is entire and unbroken, excepting at the back, from which the small fragment of bone above mentioned has been detached. The thickness of the epiphysis at its ulnar border, is nearly a quarter of an inch; at its outer border, including the styloid process, it is three-quarters of an inch.

The periosteum being firmly attached to the epiphysis and loosely adherent to the diaphysis is usually torn anteriorly at the line of separation. Posteriorly the periosteum, while remaining attached to the epiphysis, is stripped away from the posterior surface of the diaphysis.

TREATMENT

Many cases show no displacement and reduction is unnecessary. A posterior splint, preferably plaster-of-Paris, should be applied to protect the extremity from the possibility of further injury.

In those instances with any appreciable displacement or with tilting of the epiphysis, reduction should be attempted under anesthesia. In most of the recent cases this is readily accomplished by the same methods used in reducing fractures of the lower radius. A posterior moderately flexed molded plaster splint is usually sufficient to maintain the reduction. Occasionally, however, particularly in cases seen late, it is impossible to obtain full reapposition of the fragments.

In some few instances, although reduction may be easy, it is difficult to hold the epiphysis in place unless the wrist is kept in marked ventral flexion, a position described by Zadek who recommends using 100 degrees of palmar flexion in all cases.

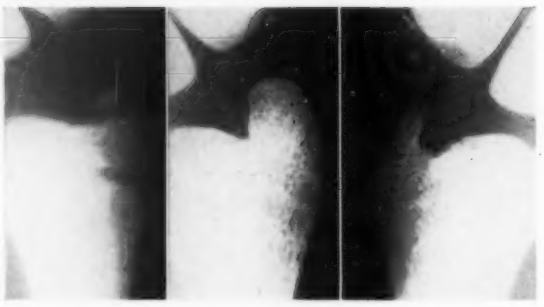
In the present series it was felt necessary to use this position of marked flexion in but a very few instances.

Union is usually solid in from two to three weeks.

COMPLICATIONS

Of the 57 separations examined roentgenographically, fracture of the styloid process of the ulna was present 29 times, an incidence of 50 per cent. Fracture of the shaft of the ulna at its lower end was present 7 times, an incidence of 12 per cent. The latter were all in younger patients.

In 2 instances, as before stated, the diaphysis was compounded on the anterior surface of the wrist. One of these patients died from gas gangrene, the only case terminating fatally.



A *B* *C*

FIG. 3. *A*. Fracture of tip of the styloid process of the ulna. *B*. The same bone five years later showing thickening and elongation of the styloid process. *C*. Styloid process of the uninjured wrist.

Nerve and blood vessel injuries were not present in this group but they do occur.

Longitudinal fractures of the epiphysis involving the articular surface are also very rare but several such cases have been reported.

Non-union apparently does not occur. No case has ever been reported.

SEQUELAE

Of the 35 injuries followed there was an accompanying fracture of the styloid process of the ulna in 16. Eight, or 50 per cent, were reunited and the other 50 per cent showed non-union at the time of the second examination. No case showed any pain or disability remaining referable to the ulnar styloid.

Whether union occurred or not, in almost every case (15 out of 16 cases) there was a thickening and elongation of the styloid process (Fig. 3).

These changes might conceivably be of practical importance in that the disturbed relationship between the styloid processes of the radius and ulna could easily mislead an examining physician into suspecting shortening of the radius rather than the true condition of elongation of the styloid process of the ulna. Roentgenographic examinations of both wrists would of course reveal the true condition. Likewise an elongated and thickened styloid process of the ulna, observed on a roentgenogram, is strong circumstantial evidence of a previous fracture.

Appreciable shortening of the radius was present in 5 of the 35 epiphyseal injuries in which a follow-up examination was obtained, an incidence of 14 per cent. All were in boys. One patient in whom the separation was bilateral developed shortening in one arm. Another patient with a bilateral lesion developed deformity in both arms. The 5 instances of shortening which occurred in 4 cases are of sufficient interest to mention briefly.

CASE I. G. P. At the age of eleven, the patient fell from a ladder striking the palm of the right hand on the ground. A roentgenogram at this time showed the epiphysis to be displaced backward 4 mm. There was no tilting present. Reduction was not attempted, a posterior wood splint was applied. Three years, one month later both wrists were roentgenographed and the right radius was 4 mm. shorter than the left. The right radius was not thickened in the anteroposterior diameter and the epiphyseal line showed no evidence of fusion. There were no clinical symptoms and the patient was unaware of any deformity.

CASE II. R. P. At the age of twelve years, ten months the patient fell from a tree to the ground, a distance of from 10 to 15 feet. A roentgenogram made at this time showed the epiphysis of the radius to be displaced backward completely with marked deformity. The tip of the ulnar styloid was also fractured. Under gas anesthesia a good reapposition was obtained and a plaster cast applied. Four years, seven months later the patient was again examined. A deformity of the right wrist was at once apparent by direct inspection. The lower end of the ulna was very prominent and the hand showed radial deviation. Roentgenographic comparison of both wrists showed the right radius to be 9 mm. shorter than the left. The epiphyseal lines in both wrists were still present and were of equal width. Except for a slight limitation of motion in ulnar deviation the function was very good and there were no subjective symptoms.

CASE III. R. E. At the age of eleven years, three months this boy fell about 20 feet from a tree striking the ground with both arms outstretched. The attending physician placed both

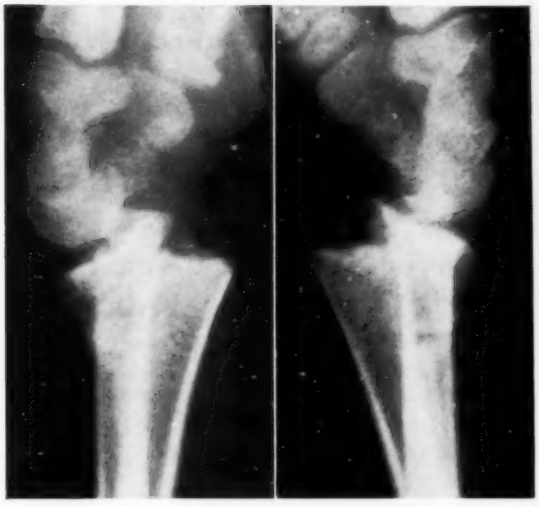


Fig. 4. Case IV. Lateral roentgenograms of left and right wrists when first seen three weeks after injury.

wrists in plaster splints. Roentgenograms made through the casts showed on the left that the epiphysis had separated with the usual accompanying wedge-shaped fracture of the diaphysis. No displacement was present. On the right the epiphysis was displaced backward 8 mm. Manipulation under roentgenoscopic control was done several days after the original injury and while the position was improved complete reapposition could not be accomplished. When examined eight years, three months later at the age of $19\frac{1}{2}$ years the epiphyses of both wrists had fused. The right radius was 7 mm. shorter than the left and slight deformity was found on clinical examination. The patient was not

Fig. 5. Case IV. Appearance after unsuccessful attempt at reduction.

aware of any difference in the two arms and had no subjective symptoms in either wrist.

Case IV. E. K. At the age of eleven years, ten months this boy was pitched from a wagon, falling on his outstretched forearms. His parents did not consider his injuries serious and a physician was not consulted until three weeks later. Roentgenograms were then made (Fig. 4) which showed marked posterior displacement and tilting of the epiphysis on either side. Manipulation with a Thomas wrench was done with but only slight improvement in the position of the fragments (Fig. 5), the epiphysis on either side being 10 mm. posterior and 10 mm. lateral to its normal position in relation to the diaphysis of the radius. The patient was again examined and roentgenographed seven months later (Figs. 6 and 7). In comparison with roentgenograms of normal wrists in a child of the

Fig. 6. Case IV. The right wrist seven months later showing remarkable improvement.

Fig. 7. Case IV. The left wrist seven months later showing similar improvement.

same age there appeared to be about 5 mm. shortening on the left and 10 mm. shortening on the right. In spite of the existing deformities the reparative changes that had taken place in seven months were astounding. Both epiphyseal lines were of normal width and showed no evidence of premature fusion. The wrists were of almost normal thickness with a remarkable range of motion. While there was definite deformity present on both sides the patient had no subjective symptoms referable to his wrists.

It should be noted that in each of the above 4 patients, as well as in all others that have come under my observation, in no instance was there any significant disability or remaining subjective symptoms following separation of the lower epiphysis of the radius. In 2 instances the patient was unaware of the existence of a mild deformity.

While the original displacement was marked in Case II, good reapposition of the fragments was obtained, yet arrest of growth occurred. Other patients receiving equally severe injuries did not develop a deformity. Again, while not present in this series, arrest of growth following separation may occur without any original displacement (Massart and Cabouat).

In 4 of the 5 instances of shortening in this group full reapposition of the epiphysis was not obtained. While no positive statement can be made from so few cases, it is suspected that incomplete reapposition of the fragments plays a part in the development of deformity; this, in spite of the fact that several cases with as much displacement appeared entirely normal at the second examination.

Case IV demonstrates the remarkable ability of the lower epiphysis of the radius to overcome a vicious union in poor position, so that both appearance and function approach the normal.

Goyrand, Hutchinson, Poland, Massart and Cabouat, Smith, and Beekman have each observed cases with similar vicious union in poor position in which the deformity practically disappeared within a few years.

Retardation of growth appears to be the rule in those rare cases with a longitudinal fracture of the epiphysis and in which the cartilage must necessarily be injured.

Smith and Watson have each reported a case of this type, both of which developed shortening. Certainly this statement is true of similar longitudinal fractures of the lower epiphysis of the tibia as reported by McFarland.

CONCLUSIONS

Traumatic separation of the lower epiphysis of the radius with an incidence of 22 per cent of the bony injuries in the region of the wrist before the closure of the epiphysis is important, first because of its frequent occurrence and second because of the possibility of resulting arrest of growth which in this series occurred in 14 per cent of the separations.

It seems logical to assume that retardation of growth or premature fusion in some instances is directly due to temporary or permanent damage to the proliferative cells of the epiphyseal cartilage.

Lack of full reapposition of the epiphysis after displacement seems to play a part in the development of shortening in some instances.

Excepting those rare instances of longitudinal fracture of the epiphysis which from the very nature of the injury are prone to develop arrest of growth, there is no way to predict either from a clinical or roentgenographic study whether or not deformity will develop, or if present will disappear in time.

In all cases with displacement seen early reduction under anesthesia should be attempted. In those cases seen late in which vicious union has occurred reduction should not be attempted, for, aside from being likely to be unsuccessful, it may further injure the epiphyseal cartilage so that it cannot overcome a deformity which it might do otherwise.

Whether there is resulting deformity or not the prognosis for a painless, useful wrist is excellent.

Coincident fracture of the styloid process of the ulna, whether union occurs or not, in the majority of instances results in thickening and elongation of the styloid easily distinguished roentgenographically.

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ROENTGEN DIAGNOSIS OF LIPOMATA*

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LIPOMATA containing sufficient fat cast sharply demarcated oval or round shadows less dense than those cast by surrounding or neighboring soft tissues and body fluids. This appearance is of great help in differentiating these tumors from other types of soft tissue neoplasms and from collections of fluid such as cold abscesses.

Bufalini,[2] in 1925, recognized the value of this finding and reproduced a roentgenogram in which a lipoma in the soft tissues of the arm showed as a radiolucent area with regular, clean-cut margins. Moriconi[7] re-emphasized Bufalini's findings and reported a lipoma of the axilla presenting a similar picture. Schulte[11] encountered a fat tumor of the forearm which caused no bone or periosteal changes but presented an area of decreased density in the soft tissues. Tagliavacche and Casanovas[12] referred to transparent shadows produced by fat tumors. Laurell[6] reported 4 cases in each of which a lipoma had been demonstrated by roentgen examination. In one of these cases (a large retroperitoneal liposarcoma) the roentgen shadow of the tumor, instead of being less dense, was denser than the shadow of neighboring soft tissues. This probably indicated that the fat content of this particular tumor was low, as Ewing[4] has pointed out, or it may mean that local increased thickness of the abdomen more than offset the greater translucence of whatever fat the tumor did contain. Two of Laurell's cases were termed "periosteal lipomata" because exostoses were noted in bone adjacent to the characteristic shadows of decreased density. Laurell described the technical factors necessary to produce the best films in these cases. Odqvist[8] mentioned that dermoid cysts with abundant fat and cholesterol stones have absorption similar to fat. He reported 2 pelvic dermoid cysts and one abdominal lipoma showing as shadows of decreased density in films. Bartlett[1] described 2 cases of lipoma which seemed to have developed from the periosteum. Although his reproductions excellently demonstrated the shadows of decreased density cast by the fat tumors, he did not mention this finding. Reiss[9] described 2 cases of intermuscular lipoma demonstrated in roentgenograms as rounded shadows of decreased density. He dealt with the differential diagnosis of soft tissue tumors and like Bufalini, Schulte and Moriconi emphasized the importance of the roentgen findings. Schinz, Baensch and Friedl[10] discussed the "fat shadow" briefly in their text and reproduced a film of Chasin's[3] showing a fat tumor of the leg.

Normally the "fat shadow" is well demonstrated in lateral roentgenograms of the knee or ankle. The subpatellar and Achilles fat pads appear as areas of decreased density sharply outlined against the surrounding tissues. Since the roentgen-ray absorption coefficient of fat is less than that of water, it is inevitable that fat should absorb less radiation than the other nonskeletal tissues because the latter are made up largely of water.

With homogeneous beams of soft radiation the absorption of heavy elements varies with the cube of the wave length and with the fourth power of the atomic number. The law does not hold for the absorption of hard radiation by the lighter elements, but the exact situation for any particular combination of elements at a given wave length can be determined by computations based on experimental absorption coefficients which are available in tabular form in physics reference books.

The atomic absorption coefficient represents that fraction of the energy falling on 1 square centimeter of any matter which would be absorbed by 1 atom of that mat-

* From the Division of Roentgenology, University of Chicago. Received for publication April 8, 1936.

ter. In a similar way the molecular absorption coefficient represents the energy absorbed by 1 molecule of the matter. Multiplying the atomic absorption coefficient by the number of atoms in 1 gram of an element gives the mass absorption coefficient of that element. To obtain the molar mass absorption coefficient of a compound, perform the following calculations:

(1) Select one of the elements in the compound and from tables in physics reference books find its roentgen-ray mass absorption coefficient.

(2) Multiply this value by the molecular weight of the element and then again by the number of times the element occurs in the compound.

(3) Repeat the process for all of the other elements in the compound.

(4) Add together the products obtained for individual elements and the sum will be the molar mass absorption coefficient of the compound. Since the molar mass absorption coefficient indicates the amount of radiation absorbed by a column 1 centimeter square and long enough to contain the number of grams indicated by the molecular weight, the mass absorption coefficient of that compound is equal to the molar mass absorption coefficient divided by the molecular weight of the compound.

Olein, one of the body fats, has a formula $C_{57}H_{104}O_6$ and a molecular weight of 884.81. For a monochromatic wave length equivalent to about 47.5 kv. (0.260 Å) the mass absorption coefficient obtained from the Handbook of Chemistry and Physics[5] is 0.185 for carbon, 0.385 for hydrogen, and 0.210 for oxygen. The atomic weights are C = 12, H = 1.008, and O = 16. By substituting these values the following expression is obtained.

$$\text{mass absorption coefficient of olein} = \frac{(0.185\times 12\times 57)+(0.385\times 1.008\times 104)+(0.210\times 16\times 6)}{884.1} = 0.211. \quad (1)$$

In a similar way the mass absorption coefficient of water is obtained:

$$\text{mass absorption coefficient of water } (H_2O) = \frac{(0.385\times 1.008\times 2)+(0.210\times 16\times 1)}{18} = 0.230. \quad (2)$$

The ratio of the entering to the emerging beam is obtained from a given thickness of material by substituting the mass absorption coefficient of a compound in the formula

$$\frac{I_0}{I} = e^{(\mu/\rho)\rho x} \quad (3)$$

where I_0 = intensity of the entering beam, I = intensity of the emerging beam, e = base of the natural logarithms, μ/ρ = mass absorption coefficient, ρ = the density of the compound, x = the thickness of the material. By dividing the ratio of the entering and the emerging radiation of one compound by the similar ratio of another compound, a comparison of the absorption of the compounds is obtained, providing both compounds have like values for x and absorption coefficients corresponding to the same wave length. The derivation of the ratio of the absorption of olein to water is as follows (equation 4):

$$\frac{\text{olein}}{\text{water}} = \frac{(I_0/I)_{\text{olein}}}{(I_0/I)_{\text{water}}} = \frac{e^{((\mu/\rho)\rho x)_{\text{olein}}}}{e^{((\mu/\rho)\rho x)_{\text{water}}}} = \exp\left\{\left(\frac{\mu}{\rho}x\right)_{\text{olein}} - \left(\frac{\mu}{\rho}x\right)_{\text{water}}\right\} = e^{[((\mu/\rho)\rho)_{\text{olein}} - ((\mu/\rho)\rho)_{\text{water}}]x}. \quad (4)$$

By substituting the calculated absorption coefficients (equations 1 and 2) and the densities of olein (0.915) and of water (1.0), the expression reads:

$$\frac{\text{olein}}{\text{water}} = e^{[(0.211\times 0.915)_{\text{olein}} - (0.230\times 1)_{\text{water}}]x} = e^{-0.0364x}. \quad (5)$$

If $x = 1$ cm., the expression solved is:

$$\frac{\text{olein}}{\text{water}} = 0.964. \quad (6)$$

This indicates that a layer of olein 1 cm. thick absorbs 0.964 as much radiation as a layer of water 1 cm. thick if a homogeneous beam of 0.260 Å is used.

Table 1 is a tabulation of the ratios of absorption of the fats to water at various wave lengths and for various values of x.

TABLE I

1	2	3	4	5	6	7		
Compound	Density	Molecular Weight	Wave Length in Å	Kv. (peak) Equiv.*	Mass Absorption Coefficient	Ratio of Absorption of Fat to Water		
						Power of e	Ratio for given values of x	
							$x=1$ cm.	$x=10$ cm.
Stearin $C_{57}H_{110}O_6$	0.862	890.7	.497	24.8	.352	$-.2075x$	.813	.125
			.417	29.6	.285	$-.1285x$	.881	.267
			.260	47.5	.213	$-.0465x$	.955	.627
			.200	61.6	.201	$-.0316x$	.968	.727
			.175	70.5	.188	$-.0284x$	.972	.754
			.146	84.5	.179	$-.0279x$	.974	.756
			.130	95.0	.174	$-.0259x$	.976	.772
Palmitin $C_{51}H_{98}O_6$	0.866	806.8	.497	24.8	.354	$-.2043x$	.816	.129
			.417	29.6	.280	$-.1322x$	.844	.269
			.260	47.5	.212	$-.0458x$	.951	.631
			.200	61.6	.200	$-.0311x$	.968	.732
			.175	70.5	.188	$-.0276x$	.973	.757
			.146	84.5	.179	$-.0275x$	.974	.758
			.130	95.0	.173	$-.0254x$	.975	.775
Olein $C_{57}H_{104}O_6$	0.915	884.8	.497	24.8	.351	$-.1895x$	.826	.158
			.417	29.6	.285	$-.1140x$	.891	.329
			.260	47.5	.211	$-.0364x$	.964	.707
			.200	61.6	.200	$-.0221x$	.977	.802
			.175	70.5	.186	$-.0203x$	.979	.816
			.146	84.5	.179	$-.0195x$	.982	.822
			.130	95.0	.173	$-.0172x$	.984	.865
Water H_2O	1.0	18.0	.497	24.8	.511			
			.417	29.6	.374			
			.260	47.5	.230			
			.200	61.6	.205			
			.175	70.5	.191			
			.146	89.5	.183			
			.130	95.0	.175			

* The voltage at which the wave length of the shortest wave in the bundle will be that indicated in column 4. The effective wave length of the beam is invariably much longer than this but it is not possible to compute its exact value from a knowledge of voltage alone. For practical purposes it suffices to note in empirical curves such as that of Hull (Fig. 1), the wave length range of the principal portion of the radiation in a homogeneous beam, compute the coefficients over this range and assume that the average or effective wave length lies somewhere between the extremes.

From the chemical standpoint the fat content of lipomata is practically identical with normal fat (Wells[13]) and should absorb roentgen rays exactly as does normal fat. However, aside from the technical details of roentgenography presently to be discussed, there are two conditions in which lipomata might fail to show as areas of decreased density in roentgenograms. First, they might contain such an abundant stroma of water-containing tissue that their total absorption would be only slightly different from that of water. Second, instead of displacing water-containing tissues they might simply lie upon them, in which case their shadows would be superimposed upon the normal shadow and might either fail to show at all or else show as areas of

slightly increased density. These two conditions necessary for visualization of lipomata must be kept in mind by those who search for them. They will be seen only if they are composed largely of fat and if they displace considerable volumes of water-containing tissue.

A study of Table 1 indicates that the differentiation between absorption of fat and absorption of water increases as the wave length becomes longer or as the tissue becomes thicker. This indicates that the best differentiation on films will occur in (1) films made with the lowest voltages possible and (2) in the larger tumors surrounded by enough other soft tissue to supply contrast. It is conceivable that a lipoma might be so small or surrounded by so much other tissue that it could not be demonstrated as a shadow of decreased density.

The calculations and discussion given above deal with homogeneous radiation but the same principles apply to heterogeneous beams. When a roentgen tube operates at 50 kv. the wave length of the bulk of the radiation ranges from about 0.25 Å to 0.4 Å, and at 90 kv. the major portion varies from approximately 0.15 Å to 0.35 Å (see Fig. 1). Since the comparative absorption of fat to water is less than one throughout the range from 0.497 Å to 0.130 Å (Table 1) it can be stated that the comparative absorption of these substances for any heterogeneous beam generated at from 25 to 95 kv. will be less than one.

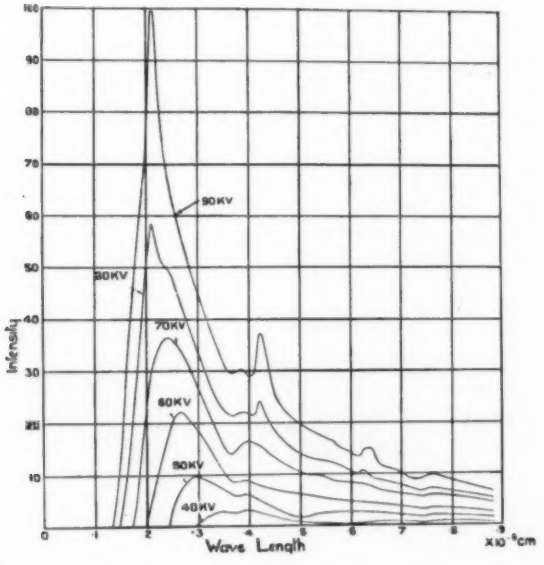


Fig. 1. Roentgen-ray spectrum of tungsten at various voltages and same milliamperage, no filter, sodium chloride crystal (by Hull).

Fig. 2. Case 1. The large shadow of decreased density about the greater trochanter proved at operation to be lipoma.

Four cases demonstrating the value of the decreased density caused by intermuscular fat tumors are presented.

Case 1. H. G., female, aged sixty, entered the University of Chicago Clinics August 30, 1930, complaining of a gradually enlarging tumor of the left thigh which had been first noticed four years previously. The patient suffered no pain and complained of no symptoms other than inconvenience.

At physical examination there was a firm, rounded, definitely circumscribed mass which was not tender and which lay in the soft tissues of the lateral aspect of the thigh. It measured about 12 cm. in diameter and was not attached to the femur.

Roentgenograms demonstrated a sharply outlined area of decreased density, 14 cm. in diameter, in the soft tissues anterior and lateral to the left greater trochanter (Fig. 2). No definite diagnosis was made by the roentgenol-

FIG. 3. Case II. Lipoma deep in soft tissues of right forearm. Proved at operation.

ogist at that time. The clinical diagnosis was sarcoma.

At operation, September 10, 1930, an intermuscular lipoma was found. It measured 16 cm. in diameter and was quite buoyant in water. Subsequent study of the roentgenograms revealed that the correct diagnosis could have been made from the films.

CASE II. J. M., female, aged fifty-nine, entered the King County (Harborview) Hospital, Seattle, Washington, August 1, 1935, complaining of a painful swelling of the right forearm. The condition had first been noted the previous winter and seemed to be aggravated by use and by weather changes. During periods of pain there was difficulty in straightening and relaxing the fingers. The patient had never noted any numbness of the hand.

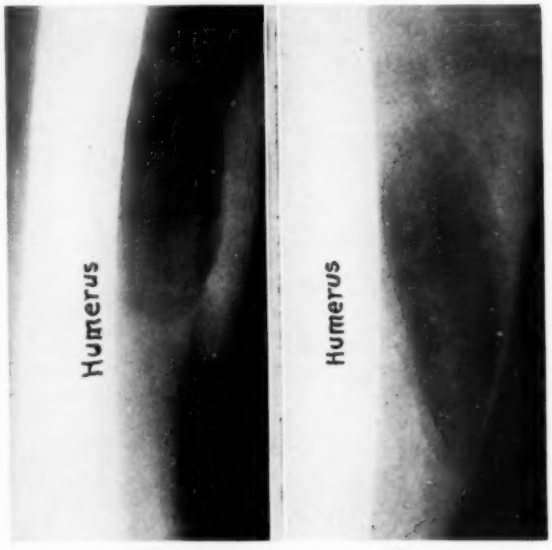
Physical examination revealed a mass, 7×7 cm., in the right forearm, just below the elbow joint. The mass was equally distributed between the extensor and flexor surfaces and rotated somewhat with the radius. On contraction of the muscles, the mass assumed the consistency of contracted muscle and seemed to move in the deeper structures. It was not attached to the skin. Although the mass seemed to rise in the soft tissue when the muscle was stretched, it was believed that it lay beneath the superficial structures. The radial pulse was palpable and equal to that of the opposite side. There were no enlarged axillary glands but the thyroid was enlarged and nodular. A tentative diagnosis of sarcoma was made.

Roentgen examination showed an area of decreased density in the soft tissues of the anterior and lateral portions of the right forearm, sharply demarcated from surrounding tissue and measuring 4×4.5 cm. The adjacent bone was not involved (Fig. 3). A diagnosis of deep-seated lipoma was considered.

On August 17 an incision through the posterior lateral aspect of the forearm, parallel to the radius, revealed an encapsulated lipoma lying between the flexor and extensor muscles. The tumor was easily enucleated. The surgical-pathological report described a lipoma measuring 8×4 cm.

CASE III. R. S., female, aged forty, entered the University of Chicago Clinics October 19, 1930, complaining of a painless oval swelling deep in the soft tissue of the posterior portion of the left arm. The patient had first noticed the swelling two weeks prior to admission. There were no other complaints except for some pain in the right shoulder.

Physical examination revealed a soft oval swelling extending along the sides of the triceps muscle deep in the soft tissue of the left arm. The mass was movable on the humerus and be-



A *B*

FIG. 4. Case III. Lipoma in the soft tissues of the left arm. The narrow streak of increased density running through the center of the tumor (seen in *B*) is probably fibrous tissue or muscle. Proved at operation.

came quite firm when the triceps muscle was contracted so it was believed that it lay between humerus and triceps. No tumors could be palpated elsewhere in the body.

Roentgenograms of the lower two-thirds of the left arm demonstrated a sharply outlined mass of decreased density lying in contact with the posterior surface of the humeral shaft (Fig. 4). It was fusiform and measured 12 cm. in length and 22 mm. in width. The proximal 3 cm. of the lesion appeared as a narrow tailed-out process. This proximal tip lay in contact with the humeral shaft at about the junction of the proximal and middle thirds. The long axis was directed distally and posteriorly to reach the lower surface of the subcutaneous fat about 9 cm. from the elbow joint. A narrow stem of denser tissue extended longitudinally through most of the mass. It was suggested that this might be fibrous tissue, muscle or fascia. A diagnosis of intermuscular lipoma in the extensor surface of the left arm was made. The mass was removed surgically and proved to be a lipoma.

Case iv. N. H., female, aged forty-seven, was admitted to the University of Chicago Clinics May 28, 1935, complaining of a painless swelling in the left arm just below the shoulder. It had been noted for eight months. The history otherwise was irrelevant.

Physical examination revealed that in the region of the acromion process there was a mass, 7×5 cm., which seemed to be beneath the muscle. It was soft but became firm when the muscles were contracted. The clinical diagnosis was sarcoma of the soft parts of the upper left arm.

Roentgenograms revealed no lesion of the left humerus except two small areas of decreased density in the upper end, the nature of which was not known. In the soft tissue about the upper end of the left humerus there was a large, sharply circumscribed, translucent area, measuring 6 cm. in diameter (Fig. 5). A diagnosis of lipoma beneath the deep fascia was made.

At operation there was found a large lipoma divided into five lobules, the largest of which measured 7×5×3.5 cm. and the smallest 1×2 cm. The tumor lay between the deltoid and pectoral muscles.

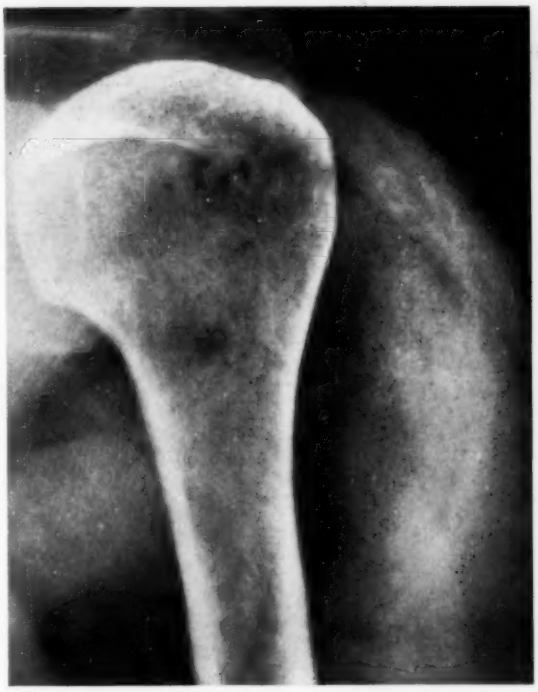


Fig. 5. Case iv. A lipoma in the soft tissues of the shoulder, casting a faint shadow of decreased density. Proved at operation.

DISCUSSION

These cases illustrate the importance of recognizing the "fat shadow." In Case i an incorrect diagnosis of soft tissue sarcoma was made. In the light of our present knowledge, this case should have been correctly diagnosed. In Case ii the clinical impression had been sarcoma but the roentgenogram had raised the question of lipoma even before operation was done. In Cases iii and iv there was a definite preoperative diagnosis of lipoma based on the roentgen findings. The strand of denser tissue seen in Case iii was probably fibrous tissue. Perhaps it was a similar contrast between fibrous tissue and fat that allowed Bartlett to visualize the stroma in his cases and led him to emphasize the importance of stroma visualization in lipomata.

SUMMARY

1. When lipomata are wholly or partially surrounded by non-fatty soft tissue, they cast sharply defined roentgen shadows of decreased density, which allows them to be differentiated from other types of soft tissue neoplasm and from collections of body fluids. This finding is particularly

helpful in the diagnosis of lipomata situated beneath the deep fascia where they are likely to be confused with sarcoma.

2. Four cases of deep-seated lipoma are presented. In one of these cases, seen before we had come to recognize that fat in lipomata casts shadows of decreased density, an erroneous diagnosis was made. We would not repeat that mistake today. In the other three cases roentgenograms definitely established the diagnosis of lipoma.

Gratitude is expressed to Dr. D. V. Trueblood of Seattle, Washington, for the use of Case II in this report.

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Vol. 37, No. 2

OBSTRUCTIVE EMPHYSEMA AND ATELECTASIS IN ACUTE RESPIRATORY DISEASE OF INFANTS*

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ROENTGEN examination of the chest in young infants with acute pulmonary disease frequently shows only minute patches of density of the lung. In fact, the severity of the illness, especially the cyanosis and respiratory distress, is far out of proportion to the apparent extent of involvement. In such cases we have been able to demonstrate by roentgen study obstructive emphysema of considerable degree. We feel that various obstructive phenomena occur in the bronchial tree with acute pulmonary disease which are of utmost importance for the understanding of the mechanism of this disease, its physical signs, symptoms, and treatment.

Roentgen examinations of 70 infants under one year of age with the clinical diagnosis of pneumonia were studied. In almost all cases varying degrees of emphysema were recognized. In many cases, especially in infants under six months of age, this was so extreme as to cause marked displacement of the heart, rotation of the heart, or depression of the diaphragm. It is our experience, based on the observation of many cases of pneumothorax, that a slight positive pressure in one side of the chest is not sufficient to displace the mediastinum, even in the absence of previous disease of the mediastinum. It was therefore obvious that portions of the lung were enlarged and under great tension. Some showed only small patches of lung density, but the emphysema involved almost all of the remaining lung. Since these last infants were extremely cyanotic and suffered severely it occurred to us that we were dealing with an extensive obstructive emphysema. If this were compensatory in a useful manner, as had been claimed, it should help aeration and diminish the symptoms.

We found by autopsy study of infants who died of pneumonia that the nonaerated portions were not infrequently scattered throughout both lungs with a predilection for the posterior and dependent portions. Emphysematous areas were likewise scattered throughout both lungs, but tended to be located anteriorly. We have been able to inflate many of the nonaerated portions of the lung at the postmortem table proving that they were atelectatic. Holt,[1] on the basis of autopsy study, likewise notes that emphysema is one of the regular and striking features of what he terms bronchopneumonia of infants. However, he believes this to be compensatory. Wessler and Jaches[7] recognize that the adjacent areas of emphysema add to the pediatrician's difficulties in the diagnosis of bronchopneumonia. Stoloff[5] likewise speaks of compensatory emphysema in pneumonia of infants and children.

We feel that the changes in aeration of the lung seen at autopsy and demonstrated by roentgen examination are caused by valvular effects in the bronchial tree, secondary to inflammatory reactions and secretions in them. Dr. Solomon Weintraub, the Pathologist at Harlem Hospital, confirms our findings of atelectasis posteriorly and emphysema anteriorly, by histological study.

In 1920 Manges, together with Jackson and Spencer,[2] described for the first time obstructive emphysema of the lungs with aspirated non-opaque foreign bodies in the bronchial tree. In the early stages of this condition the foreign body acts as a ball valve. During inspiration the bronchus opens and allows air to pass. During expiration the bronchus contracts to rest on the foreign body and blocks the outflow of

* Material for this paper collected from the Harlem Hospital and The Bronx Hospital, NewYork City. Read before the New York Roentgen Society, April 20, 1936.

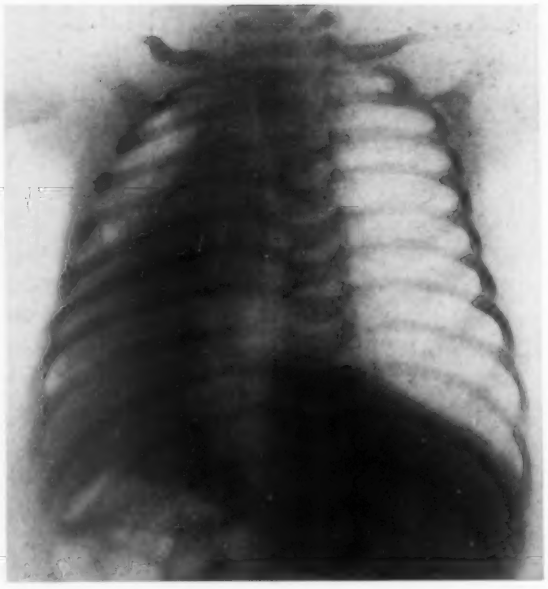

FIG. 1. Clinical diagnosis: Bronchopneumonia. Marked cyanosis. Roentgen findings: Mediastinum displaced to left, right diaphragm forced downward. Right intercostal spaces widened. Roentgen diagnosis: Obstructive emphysema right lower lobe in acute respiratory disease.

air. Jackson, in particular, recognized that this mechanism was enhanced by the accumulation of secretions and pus.

Keeping in mind the work of Manges and his coworkers, our findings with the roentgen studies, and our experience with autopsy material, the problem clarifies itself. The lumina of the bronchial tree of infants are very small, even the main branches. With acute respiratory disease pus and secretions collecting in them are more likely to cause obstructions. Since the infant is kept on its back, gravity carries most of this material into the dependent parts of the branches. The anterior branches are only partly filled. As a result of this situation, complete obstructions or blocks tend to take place posteriorly, giving rise to patches of atelectasis. Ball-valve effects develop anteriorly, giving rise to obstructive emphysema. It is obvious that as the secretions and pus are shifted by ciliary movement, cough, changes of posture, and new accumulations, the atelectases and emphysemas may also shift. This may be rapid and often gives rise to contradictions between the various examiners, the roentgenologist, and the pathologist. Emphysematous areas may become completely blocked and go on to atelectasis. We have seen emphysematous blebs at autopsy which had ruptured. With a ball-valve action of a small bronchus sufficient tension of the trapped air may develop to produce this effect. This explains why we have found spontaneous pneumothorax by roentgen study in some of our cases of pneumonia. In others, it seems to be due to rupture of a cortical abscess of the lung and usually results in an emphysema.

We are not primarily attempting to prove where the infection of the lung starts, but we feel that once the disease has set in, the obstructive phenomena predominate the picture. Inspection of the roentgenogram may show only very small patches of density which are deceiving if the degree of emphysema is not considered.

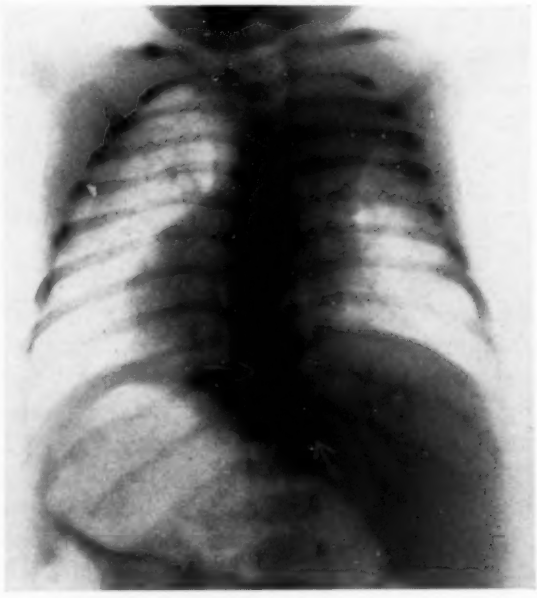

FIG. 2. Clinical diagnosis: Pneumonia. Roentgen findings: Right lower lobe over-distended reaching into the left chest. Left lower lobe over-distended to a lesser degree. Right upper lobe non-aerated and contracted in size. Roentgen diagnosis: Obstructive emphysema right and left lower lobes. Atelectasis right upper lobe. Pneumonia may also be present here.

To understand the severity of the symptoms the obstructive emphysema described by us must be considered as a very important part of the picture. The sudden development of cyanosis can easily be explained by a block of a large portion of the bronchial tree, regardless of whether this leads to atelectasis or obstructive emphysema.

The treatment of pneumonia or bronchitis in infants must be directed at clearing the bronchial tree in addition to other methods of attack. This is equivalent to the establishment of free drainage, a principle well recognized in therapy. Every effort must be made to thin out the accumulations in the bronchi and to get rid of them. The older clinicians frequently relied upon syrup of ipecac and ammonium carbonate which they often gave to the point of nausea and vomiting. They claimed that this cleared the system. Judging by our findings they appear to have been correct. Strychnine suggests itself as of value because it would increase the sensitivity of the cough reflex. Warfield[6] states that he had very favorable results with this drug during the influenza epidemic because it helped him to control the blood bed and therefore the shock of acute systemic infections. It would appear that this drug may yet return to popularity. Since a tremendous portion of the lung is out of function, as has been described, the favorable results with oxygen can be understood. However, this paper is not primarily concerned with therapy, but rather to show that a rationale for the symptom-complex of acute respiratory disease of infants must in great measure be based on the factors we have described.

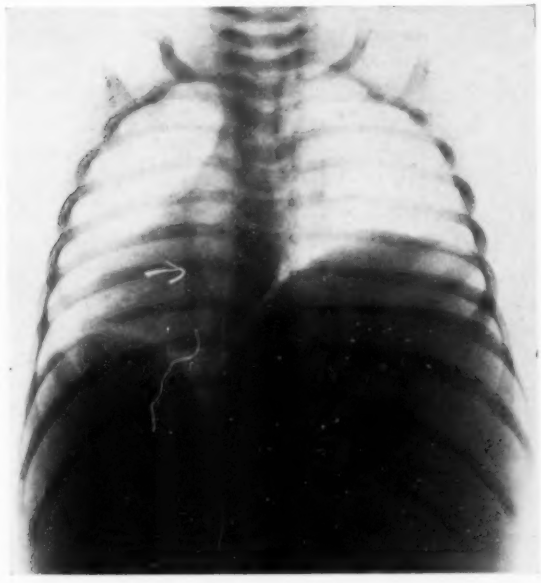

Fig. 3. Clinical diagnosis: Pneumonia. Roentgen findings: Right upper lobe over-distended reaching into the left chest. Mediastinum displaced to left. Intercostal spaces spread right upper, narrowed right lower regions. Right diaphragm elevated. Roentgen diagnosis: Obstructive emphysema right upper lobe. Atelectasis right lower lobe in acute respiratory disease.

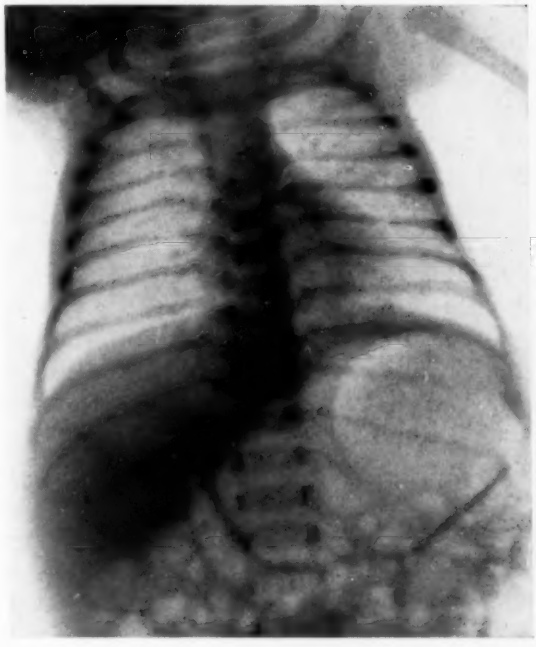

Fig. 4. Clinical diagnosis: Bronchopneumonia. Roentgen findings: Inner border right lower lobe reaches into left chest. Superior mediastinum has narrowed appearance due to over-ventilation of the medial borders of both upper lobes. Roentgen diagnosis: Scattered obstructive emphysema right and left in acute respiratory disease.

SUMMARY

1. Bronchial obstructions, complete and partial, are of utmost importance to the understanding of acute pulmonary disease of infants.

2. We have shown that obstructive emphysema is a very important factor.

3. This may be so widespread that very little functioning lung remains.

4. In the very young infant this emphysema is a predominant factor and largely accounts for the cyanosis and severity of the symptoms.

5. The rapid shift of physical signs, which is so commonly observed, simply means that a shift in the accumulations in the bronchial tree has taken place.

6. The distribution of consolidation or atelectasis posteriorly and obstructive emphysema anteriorly is explained on a mechanical basis. Gravity carries most of the secretions posteriorly giving complete block to the bronchi. The bronchi anteriorly being only partly filled tend to develop a ball-valve obstructive emphysema.

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Vol. 37, No. 2

ROENTGENOLOGIC EVIDENCE OF RAPIDITY OF GROWTH IN GASTRIC CARCINOMA*

REPORT OF CASE

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THE main object in reporting this case is a roentgen demonstration of the rapidity of a malignant tissue destruction.

A male, aged fifty-three, has been under my observation since 1922. The presenting symptomatology at that time was a hyperacidity syndrome with marked aerophagia. The clinic record (Vanderbilt Clinic, Columbia University) showed in 1922 and 1924 that gastric analysis revealed anacidity. A roentgenologic investigation of the gastroenteric tract disclosed negative findings, except for spastic constipation. The achylia gastrica has since proved to be true to histamine.

The recent symptomatology (March, 1936) was of a varied character because of an associated neurosis. Essentially, however, the symptoms were those of a reverse peristalsis syndrome (Alvarez). The physical findings were basically negative, except for hypotension. The blood cytology was negative, and red cell sedimentation revealed a horizontal line, indicating a clinically healthy individual. The roentgen study (March, 1935) of the gastrointestinal tract revealed no abnormality. Cholecystographic findings were normal. In view of the gastric anacidity and persistent dyspepsia syndrome, diagnostic biliary drainage was resorted to. No food residue was found in the fasting stomach. The tube was permitted to descend to the fourth ring. Aspirates recovered by gravity method, showed a 2 plus flocculation. Microscopy indicated that the flocculi were loaded with white blood cells, pus cells and desquamated epithelia, some in clumps, many discrete. Each miscroscopic field presented the same picture. Suddenly frank blood flowed freely. The patient, a hyposensitive individual, was not alarmed at the sight. A syringeful of cold water was injected, and after a few minutes the bleeding stopped. Since no syringe suction was used and all aspirates were recovered by syphonage, the appearance of blood merited attention. As no bile-stained cellular evidence was noted, extrahepatic pathology was a justifiable deduction, and a roentgen investigation of the gastrointestinal tract was undertaken. The report (November 7, 1935) read: "Irregularity of the pyloric end of the stomach, suggesting a malignancy." Another roentgen examination sixteen days following this study disclosed a persistent filling defect with canalization involving the pyloric third of the stomach, and a small residue five hours following ingestion of the barium further demonstrated canalization.

The patient was operated upon (November 29, 1935) by Dr. Walter Gray Crump. A malignant mass involving the pyloric segment was removed, a Billroth I performed. No metastasis was found.

The pathological diagnosis was "double chronic gastric ulcer with glandular and anaplastic carcinoma."

Comment. The literature is filled with divergent opinions concerning early diagnosis of gastric cancer. The roentgenologist maintains that early diagnosis is his task; the internist holds that early diagnosis of gastric cancer is made from the symptomatology and the anamnesis. Rehfuss,[1] in his review of the book by Moutier, draws attention to the fact that the author believes roentgen study is not a means of early, but rather of late diagnosis in gastric carcinoma. To this I fully agree. "We feel," writes Rehfuss, "that this statement might be put the other way and that is, that the diagnosis is due to the fact that the disease is so silent and latent in the early stages that in the great majority of instances when

[1] Rehfuss, M. E. Review of Moutier, F. Traité de gastroscopie et de pathologie endoscopique de l'estomac. Masson et Cie, Paris, 1935. In: *Am. J. Digest. Dis. & Nutrition*, November, 1935.

* From the Gastroenterological Department of the New York Medical College and Flower Hospital.

Fig. 1. Normal gastric outline, March, 1935.

the patient reaches us the lesion already is far advanced." I believe that the expert roentgenologist is able to detect a malignant lesion at a stage when the lesion is still resectable, but this implies advanced pathology. A beginning malignancy is hard to discern by mechanical methods of approach. The case under discussion was roentgenographed in March, 1935, perhaps the right time for early diagnosis. This was not obtained because of the negative roentgen findings (Fig. 1) and a protean symptomatology. The laboratory findings also made a diagnosis of malignancy seem improbable. If the cancer then already existed the roentgen study failed to disclose an early lesion. The appearance of an "irregularity of the pyloric end" as revealed on November 7 (Fig. 2) was to be reinterpreted in the light of an indefinite clinical picture of malignancy, a negative blood cytology, a negative blood Wassermann, and a normal rate of red cell sedimentation; inasmuch as it is held that tissue destruction is the cause of rapidity in sedimentation, the normal curve at this time made it a fair surmise that the lesion was in an early form that developed into a demonstrable lesion during a period of sixteen days (Fig. 3). Rapidity of growth must be considered the outstanding feature.

Fig. 2. Irregularity suggesting malignancy, November 7, 1935.

Fig. 3. Filling defect with canalization, November 23, 1935.

What impresses me as important and admonitory is that while a patient with achylia need not be given the idea that he has cancer, the clinician must be cancer minded all the time. The sole case here re-

ported is in disagreement with Bloomfield and Polland[2] who concluded from a study of a group of patients in whom the histamine refractory chemistry was unexplained that in no case did the achlorhydria furnish a fertile soil for cancerous implantation.

We have here then a case of primary carcinoma that ulcerated. This opinion is based on the following: (1) a history of true achylia, probably congenital, since nothing was elicited in the history to suggest an acquired atrophic gastritis; (2) in a section from the deeper portion of one ulcer, numerous mitotic figures and atypical glandular tissue were found; (3) microscopic section of the wall and base of the second ulcer showed the base to consist almost completely of atypical cell growth.

There are many factors involved which tend to cause a late diagnosis of gastric cancer, but those to be emphasized are: economic status of the patient (preventing frequent roentgen investigation), his mental reaction to physical aberration, the all too often latency of the malady, and a relative suddenness of onset and rapidity of progression. In my opinion, a patient with achlorhydria should be under constant clinical observation with the thought of detecting early gastric cancer. Degenerative rapidity in a case of true achlorhydria is well demonstrated in this present instance.

[2] Bloomfield, A. L., and Polland, W. S. The fate of people with unexplained gastric anacidity; follow-up studies. *J. Clin. Investigation*, 1935, *14*, 321–324.

PROTRACTED IRRADIATION BY RADIUM*

By HAYES E. MARTIN, M.D., F.A.C.S., *and* WILLIAM S. MACCOMB, M.D.
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THE principle of protracted or fractionated dosage in radiation therapy is at the present time rather generally accepted as being preferable to the massive dose method in the treatment of many forms of cancer. Although it has extended the range of curability of certain tumors by irradiation, highly fractionated or protracted dosage has the disadvantage of being a more complicated, time-consuming and expensive procedure than the massive dose method. The control of many of the small accessible growths of the skin and mucous membranes presents a few difficulties by the simpler single dose method, and in these or in similar situations, protraction of dosage is, in our opinion, neither necessary nor particularly advantageous.

For practical purposes, protracted irradiation must be considered in a limited sense, since there are infinite possibilities of variation in the total treatment time and in the number and spacing of unit doses. In this discussion, therefore, we will arbitrarily confine the meaning of the term to the practical present-day usage. The total treatment time for this form of treatment in our clinic is preferably twenty to thirty days or longer, and never less than ten days. The individual treatments to the same volume of tissue are preferably given daily, in some cases (as a matter of convenience) every other day, and in other rare instances twice a week. Under certain conditions, which we shall discuss presently, the exposure may be continuous.

Following the original investigations by Coutard, most observations on fractionated dosage have been limited to roentgen rays, but it must be admitted that if the principle of protraction is correct, it should apply to gamma rays as well as to roentgen rays, and to the intracavitary and the interstitial as well as to the external application of radiant energy. It is with the protracted application of gamma rays, especially from intracavitary and interstitial radiation, that this discussion is particularly concerned.

GENERAL CONSIDERATIONS

There has been considerable discussion in the published reports as to the relative importance of such variable factors as intensity and total treatment time. Coutard and many others believe that a low intensity (4 ma., 3–4 r/min.) and a longer total exposure time is far superior to a high intensity (30 ma., 40–60 r/min.) and a shorter exposure time.† While admitting the possibility of the truth of such a contention, nevertheless in our experience, we have not observed any marked difference in the biological effects of comparable fractionated doses delivered at 30 and 4 ma. If, however, the time-intensity factor is of the importance its proponents believe, then the *ideal* type of radiation would be of such low intensity as to be given continuously over the desired treatment period (ten–twenty–thirty days). Obviously, such continuous irradiation to a limited tissue volume can be administered only by radium.

Fractionated therapy by radium must ordinarily be of lower intensity than by roentgen radiation—a natural consequence of the high cost and limited quantity of this element. This fact is a serious disadvantage in the external application of radium for deep therapy, as we shall discuss under a separate heading.

† In fractionated or protracted therapy, the exposure or treatment time during which the patient is exposed to radiation should not be confused with the total treatment period. For instance, under certain conditions, radiation may be applied to a given volume of tissue continuously for two weeks. The exposure time and total treatment period in this case would be the same (fourteen days). If, however, the exposure lasted one hour daily over a period of two weeks (except Sundays), the total treatment period would still be fourteen days, but the treatment or exposure time would be twelve hours.

* From the Head and Neck Service of Memorial Hospital, New York. Read at the Twenty-first Annual Meeting, American Radium Society, Kansas City, Mo., May 11–12, 1936.

For protracted irradiation which may be given from within a body cavity or interstitially, a low intensity is essential, and the several advantages of radium are unique. By the use of radium for such purposes, one may obtain fractionated or even continuous radiation of low intensity without complete immobilization of the patient during exposure, as would be necessary with roentgen rays and radium packs. As a matter of fact, most patients may be ambulatory. If the radium element is properly subdivided into needles, capsules or cells, a wide variation in technique and unit strength is possible.

For protracted irradiation by radium, in all situations except where interstitial irradiation (radon seeds) is called for, the element, because of the constant intensity, is preferable to radon, although a fair degree of uniformity in intensity might be obtained from radon if the applicator were removed every three to five days and the original radon content restored by addition or replacement. In most cases, if radium is used, it will be found necessary to keep the patient hospitalized during treatment to avoid the danger of loss of the element. We sometimes permit the patient to be ambulatory and remain at home if he is able to furnish a bond or deposit to cover the possible loss of the radium.

We trust that the techniques which we are about to describe will prove to be of some therapeutic merit in the management of growths in certain localities, but aside from these practical considerations, we trust also that investigations such as these may eventually throw some light on the question of the importance of the time-intensity factor in radiation therapy.

PROTRACTED IRRADIATION WITH RADIUM ELEMENT PACKS

We have employed the 4 gm. radium element pack for protracted irradiation in pharyngeal cancer in certain cases since 1930. At a distance of 10 cm., a daily dose of 10,000 mg-hr. seems to produce on the skin of the neck and in the deeper tissues of the pharynx a physiological effect comparable to a daily dose of about 350 r with portals of equal size (7 cm. in diameter). By such daily dosage, these two modalities will deliver total doses of 100,000 mg-hr. ×2 and 3,500 r×2 respectively in 20 exposures, with comparable reactions in the normal and neoplastic tissues. At the completion of such total doses, additional treatment may be given, depending on the individual tolerance of the patient and the response of the tumor. Such additional treatment may be in the form of external irradiation of the same character, or by interstitial implantation.

We have attempted to compare the relative merits of gamma rays and roentgen rays in this form of treatment, but so far, we have been unable to detect any consistent difference in the physiological effects or end-results in the two methods. It is obvious that for accurate conclusions, only those cases which are anatomically and histologically similar may be used for comparison. For this purpose, single lesions of the tonsil or hypopharynx without metastases were for a time assigned to one or the other of these modalities in rotation. Successful results were obtained by both in apparently about the same percentage. The series studied for this purpose was too small to permit of any definite conclusion, but we are of the opinion that there is probably no marked superiority in the selective action of either.

The use of radium element for protracted deep therapy presents many disadvantages which are not easily overcome. The intensity of radiant energy available at any effective and useful distance is small as compared to roentgen rays. With a 4 gm. element pack and the relatively short radium-skin distance of 10 cm., an exposure time of about two and a half hours is required to deliver a dose (10,000 mg-hr.) which is about as effective biologically (on the skin) as eight to ten minutes (350 r) at a target skin distance of 65 cm. with roentgen rays at 30 ma. Distances greater than 10 cm. are hardly practicable for pro-

tracted irradiation with such quantities of radium element (4 gm.) because of the time factor, since even at 15 cm. a comparable daily exposure would require about five and a half hours. For these reasons, relatively few patients may be treated by this expensive apparatus as compared to a standard 200 kv. roentgen therapy machine at 30 ma.

Another disadvantage of the radium element pack is its lack of flexibility in certain positions such as the lower part of the neck, especially in fat subjects or in any anatomic part which requires tilting of the beam. At such short distances as 10 cm., the beam must be more or less at right angles to the skin surface in order to be both safe and effective. To parallelize a beam of gamma rays to a degree approaching that of our present day roentgen rays would necessitate distances of 25 or more centimeters and 25–50 gm. of radium. Unless a cheaper source of supply of the element is obtained, such arrangements are obviously economically impossible and furthermore, with large concentration of radium, the physical protection and mechanical adjustments of the apparatus present even greater difficulties. It is our opinion, therefore, that while protracted irradiation by element packs is of value from the standpoint of research in biophysics, it has, at this time, little practical importance in the treatment of cancer.

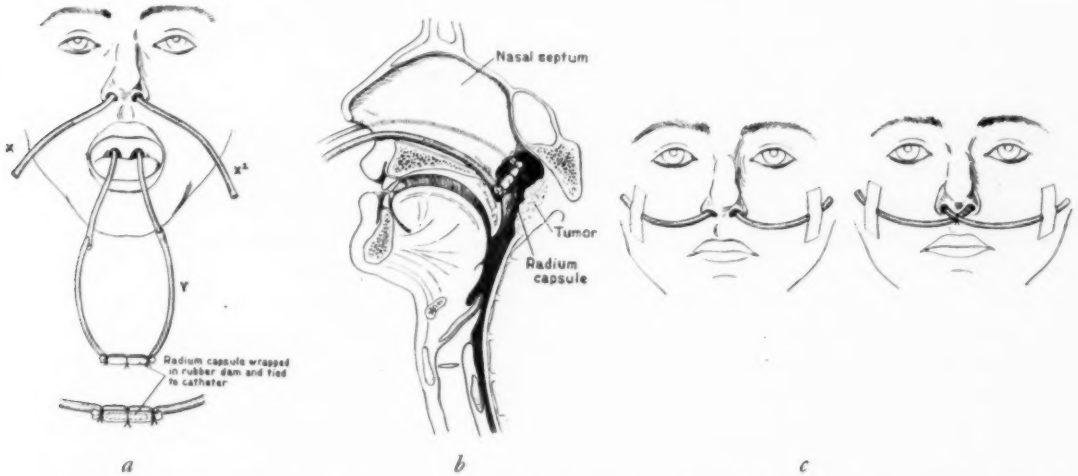
PROTRACTED INTRACAVITARY IRRADIATION BY RADIUM

Nasopharynx. An anatomic region which lends itself admirably to protracted irradiation by radium element is the nasopharynx. Growths of the nasopharynx cannot, in our experience, be efficiently irradiated by any form of interstitial implants because of the difficulty of access and the fragility of the lesions. This region may be irradiated by roentgen rays delivered through the skin of each cheek just lateral to the nose, but such treatment carried beyond doses of 3,500 r×2 is attended by several serious disadvantages. Severe skin blistering of the cheeks is not tolerated quite so well as on the neck, since the reaction tends also to involve the lower eyelids as well as the palate. However, a moderate dose of roentgen rays (2,500–3,000 r×2) may be either preceded or followed immediately by intracavitary irradiation by radium element. The combination of the two is capable of producing the desired degree of reaction within the nasopharynx without the marked undesirable effects above mentioned. In the case of late recurrence of the primary lesion in the nasopharynx after heavy roentgen irradiation through the cheeks, the skin may present such marked sclerosis as to contraindicate further roentgen irradiation to these regions. In several such cases, we have been able successfully to control the recurrence by protracted intracavitary radium application.

Intracavitary irradiation of the nasopharynx by massive doses of radium is an old procedure. We are discussing it here only from the standpoint of protracted dosage by radium which necessitates some modifications in technique. For this purpose, we have used platinum radium element needles (0.25 mm. Pt) of both 5 and 10 mg. strengths, enclosed in a capsule of lead or type-metal with a wall thickness of 1.5 mm. The total filtration in these applicators is about 1.0 mm. of platinum (equivalent). The capsules vary in size from 2–2.5 cm. in length and 4–6 mm. in diameter, depending on the size of the enclosed needles.

The capsule, as described above, is enclosed in one or two layers of rubber drain or Penrose tubing which is wrapped about it and firmly tied to the middle of a No. 14 French rubber catheter (Fig. 1*a*). The applicator is then inserted as follows: After topical application of a 10 per cent solution of cocaine to the nasal cavities and pharynx, additional rubber catheters are inserted—one through each anterior naris, and the ends pulled out from the pharynx through the mouth. The ends of the ra-

dium-bearing catheter are then tied or otherwise fastened to the ends protruding from the mouth (Fig. 1*a*) and are thereby drawn into the pharynx and back out through the nasal cavities. Assisted by digital manipulation, the capsule may then be drawn into the nasopharynx in the same manner as a postnasal tampon. The position of the capsule is carefully palpated and inspected by a throat mirror so as to be certain that it lies exactly transversely (Fig. 1*b*), just posterior to the nasal septum on the upper surface of the palate. The ends of the catheter emerging from the anterior naris are then carefully marked so that the correct position of the capsule can be subsequently determined and the two ends fastened by either one of the two methods illustrated in Figure 1*c*.



a *b* *c*

Fig. 1. *a*. Rubber catheters (*X* and *X*¹) have been inserted through each nasal cavity and pulled out from the pharynx through the mouth. A third catheter (*Y*) to which the radium capsule has been tied is then attached to these nasal catheters, which are then pulled back out through the anterior naris, so that the radium capsule enters the nasopharynx. *b*. Diagrammatic view of the nasopharyngeal capsule in place. *c*. Alternate methods of fastening the catheter ends to the skin of the face. Marks should be placed on the ends so that the correct position of the radium capsule may be assured.

When we first began the use of radium for protracted irradiation of the nasopharynx, we employed a device, which had formerly been used in our clinic, by which the radium capsule was drawn into position and held by strings or cords emerging from each anterior naris, and a third string or cord emerging from the mouth—the latter to facilitate withdrawal. This method we found to be rather unsatisfactory if used over a period of several days. The cords in the nasal cavities produced considerable trauma during their insertion and by their continued presence, even though threaded by short pieces of rubber tubing. The string emerging from the mouth also proved to be of considerable annoyance to the patient. Our present form of applicator, as described above, has been tolerated with little or no annoyance or discomfort, and is readily removed by pushing one of the nasal catheters backward until a loop appears in the pharynx which may be grasped by a forceps and the entire applicator removed.

When we first began the use of this device for protracted irradiation of the nasopharynx, we attempted to avoid undue mechanical irritation and infection by removing the applicator daily, irrigating the nose, and after a few hours' rest, re-inserting it. We soon learned, however, that the constant mechanical presence of the applicator caused very little irritation of any kind, but that the cumulative effect of the trauma of the repeated removals and reinsertions was considerable. At the present

time, we leave the radium in place for four or five days before removing it for cleansing and re-insertion. In one case the applicator was left in place continuously for ten days before removal and re-insertion without any untoward effects. Using a nasal syphon, the nasal cavities and nasopharynx may be irrigated several times a day with the apparatus in place.

Lacking precedent, at first our dosage was entirely too small. A 5 mg. capsule left in place continuously for twenty days will deliver only 2,400 mg-hr.—a dose considerably below local tolerance and which we have learned is usually insufficient to sterilize the average anaplastic growth occurring in the nasopharynx. If used alone, a dose of 3,500 mg-hr. is well tolerated if given in twenty days. Such a total dose is obtained by the use of 10 mg., leaving the applicator out for forty-eight hours every fifth day. A capsule of 7 mg. left in place continuously for twenty days would deliver about 3,500 mg-hr.

Nasopharyngeal capsules of radium are perhaps best used in conjunction with roentgen radiation, and we have recently been applying a dose of 2,500–3,000 mg-hr. in fifteen to twenty days by this means, and following it immediately by the application of 1,500 to 2,000 r to each cheek (7 cm. circular portals—350 r daily to alternate cheeks). We believe that this combination of methods is worthy of further investigation and trial.

Nasal Cavities. Many of the difficulties in the management of nasopharyngeal cancer are also found in tumors of the nasal cavities. The latter growths are usually fragile, vascular, difficult of access and present ill-defined boundaries. External radiation to the nasal cavities is best given through the skin of the nose and cheeks in about the same location as for nasopharyngeal cancer, and as a result, the same limitations in dosage must be observed and the same complications expected. For these reasons, a combination of protracted external and intracavitary irradiation is useful in avoiding the complications already mentioned in connection with the nasopharynx.

For protracted intracavitary irradiation of the nasal cavities, we have employed a 5–10 mg. radium element capsule placed in the end of a catheter or soft rubber tube whose size is as large as the nasal cavity will admit (No. 16–22 French). After careful localization of the lesion, the applicator is inserted through the anterior naris so that the radium lies directly opposite the growth and the protruding end of the catheter is then taped to the skin of the nose and upper lip. Our dosage in these cases has varied from 1,500–3,000 mg-hr. given continuously over a period of three to four weeks.

Esophagus. Intra-esophageal irradiation by the use of capsules of radium or radon has been employed in a variety of techniques for a number of years. So far as we know, Guisez[1] has published the only five-year cures by this method, employing low intensities over a protracted treatment time of ten to twenty days. The technique is rather complicated and usually requires a preliminary gastrostomy, after which the applicator is accurately placed under direct esophagoscopic vision, and firmly held in place by threads emerging from the mouth and gastrostomy stoma. The detailed technique in our clinic has been published by Dr. William L. Watson.[2] Although theoretically sound, intra-esophageal irradiation for esophageal cancer in our hands has not been as successful in palliation and prolongation of life as protracted external irradiation by roentgen rays.

Intrinsic Larynx. Cancer of the vocal cords is usually of an adult histological type, and does not respond to protracted roentgen irradiation as successfully as does extrinsic laryngeal cancer. Intrinsic cancer in its early operable stages is probably best dealt with by partial laryngectomy. We have felt that advanced intrinsic cancer not suited to partial laryngectomy is more amenable to laryngostomy and interstitial irradiation than to total laryngectomy. Our technique for laryngostomy and im-

plantation of radon seeds will be described in a subsequent report. We have recently developed a new technique for intracavitary irradiation of advanced cordal cancer, which may prove of value in certain of these cases.

In this technique, a laryngostomy is performed by our usual technique and our special laryngostomy tube with adjustable saddle is inserted. By the use of a special attachment, as illustrated in Figures 2*a*, *b* and *c*, a capsule of radium element is held within the cavity of the larynx exactly on a level with the growth. The whole apparatus is removed, cleansed and re-inserted daily. The technique is rather new with us, and we have so far used it in but one patient who has received a dose of 2,600 mg-hr. in fifteen days, after which we observed the severity of the reaction for ten days and then re-inserted the apparatus for a total of 1,000 mg-hr. in addition, making a total of about 3,600 mg-hr. in about one month. We believe this dose to have been far below the tolerance and propose to increase it in future cases.

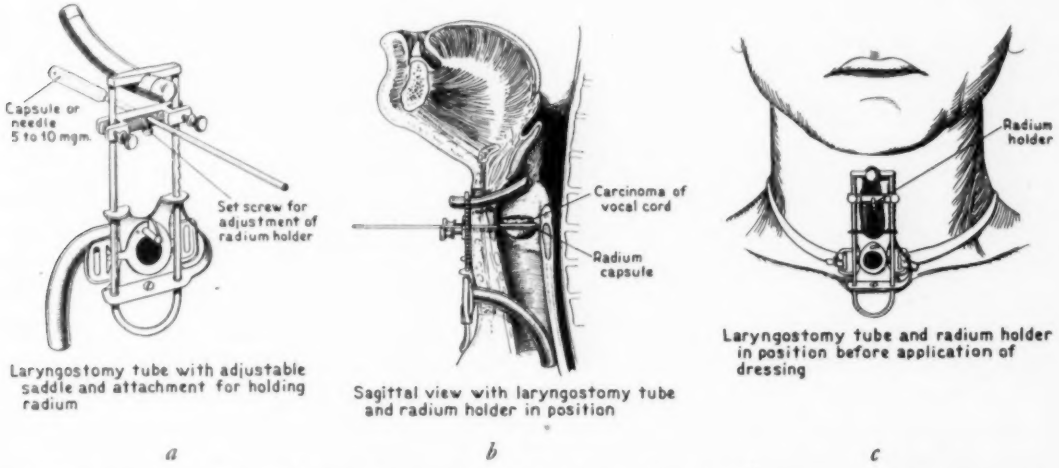

Capsule or needle 5 to 10 mgm.
Set screw for adjustment of radium holder
Laryngostomy tube with adjustable saddle and attachment for holding radium
Carcinoma of vocal cord
Radium capsule
Sagittal view with laryngostomy tube and radium holder in position
Radium holder
Laryngostomy tube and radium holder in position before application of dressing
a
b
c

Fig. 2. Laryngostomy tube with attachment for holding the radium in the larynx. *a*. Laryngostomy tube with adjustable saddle and attachment for holding radium. *b*. Sagittal view with laryngostomy tube and radium holder in position. *c*. Laryngostomy tube and radium holder in position before application of dressing.

Maxillary Antra. The ideal method of treatment of cancer of the antra is by protracted roentgen irradiation given through the skin of the cheeks. This method has been successful in a considerable number of our cases, and we have already published the technique employed in our clinic.[3] However, certain of the more radioresistant growths of the antra have, in our experience, so far resisted complete sterilization by roentgen irradiation, and in these, we have resorted to surgical exposure and intracavitary irradiation by radium.

In radium therapy of cancer of the maxillary antra, it is usually necessary to open and drain the cavity. The Caldwell-Luc operation is not suitable for this purpose, and in order to obtain adequate exposure and drainage, we prefer the removal of the floor of the antrum including a portion of the alveolus and adjacent hard palate, about 3 cm. in diameter. When interstitial radon is employed, either in massive or divided doses, the seeds are implanted a week or two prior to the drainage operation above described. In several instances of recurrent carcinoma of the antrum, we have employed small quantities of the element such as 5–10 mg. placed directly in the center of the cavity, in order to deliver a uniform dose to all portions of the cavity's walls.

A useful form of applicator for protracted irradiation of the antra after antrotomy, or

the walls of any defect in the upper jaw, may be made in the form of an obturator of vulcanized dental rubber with the radium recessed in the center, and with an incorporated lead shield to protect the tongue. In order that it may be readily placed and maintained in its correct position, the device should be molded so as to extend onto the adjacent hard palate and alveolus.

The total dose over a period of two to four weeks will depend somewhat on the size of the cavity, which will determine the distance of the radium from the walls. We have employed doses of from 2,000–4,000 mg-hr. over that period.

PROTRACTED IRRADIATION BY GOLD RADON SEEDS

The normal decay of interstitial radon provides a form of protracted irradiation which, however, has the disadvantage of a rapid decline in the initial intensity to 50 per cent in a little less than four days, and in the relatively short period of ten days the intensity has been reduced to less than 20 per cent. Obviously, such an uneven intensity and short time period fall far short of the ideal, if one desires protraction over a period of twenty to thirty days. This difficulty can be partly overcome by implanting the radon in fractions of the total dose every four to six days. The total dosage must be larger than a corresponding single unit dose. For instance, one should employ a total of 30–35 mc., if implanted in three fractions in twenty days, to care for a lesion which would have required 20 mc. implanted in one sitting. Theoretically, the first of the fractionated doses of seeds should be larger than the succeeding ones, in order to produce the greatest possible uniformity in intensity during the treatment period. On the basis of the rate of radon decay, one might calculate exactly the proper size of the several fractions of the dose, but in our opinion, such a refinement in technique would be more pedantic than practical.

By such fractionated interstitial dosage, one may obtain a physiological effect similar to that which is secured by protracted external irradiation. The method is particularly advantageous in situations such as bulky growths of the tongue, where a sufficiently large single unit dose of radon seeds is apt to cause radionecrosis. Where the necessary total dose is small, or where no complications are to be feared from large doses of implants, the principle of fractionated doses of seeds probably has little advantage.

It is a common observation that the beneficial effects of irradiation by any method in a given case will increase proportionately with the dose *up to a certain point*. Beyond this point, the law of diminishing returns operates to an increasing degree with an increase in the total dose, so that, finally, further irradiation is not only useless but harmful. This rule applies to all technical methods of irradiation. It will be found, however, that not all of the disadvantages and harmful effects of external and interstitial irradiation are identical, so that the cumulative harmful effects of a combination of less than maximum doses of the two will be considerably less, and the lethal action on the tumor greater than would be the case if either method alone were pushed to its limit of safety. The practical application of this rule is best illustrated by several examples.

Carcinoma of the base of the tongue, often presenting a bulky tumor when first seen, is not easily controlled by external irradiation alone. It will commonly be found that after the application of 3,500 r to either side of the pharynx with circular portals 7–8 cm. in diameter, the tumor will have regressed only about one-fourth to one-third, despite a marked mucositis in the pharynx. The question then arises whether to push the dose up to a higher level (4,000 r×2–4,500 r×2). In our experience, even these doses have frequently failed to produce complete regression, though the general effects on the normal tissues of the pharynx were such that recovery was slow and at times incomplete.

Since we have adopted the following technique of supplementing a moderate external dose with gold radon implants into the base of the tongue, our results have markedly improved. At the present time, we never give more than 3,000–3,500 r to each side of the pharynx in cancer of the base of the tongue. Immediately on the completion of the external irradiation, radon seeds in doses of about 10–20 mc. are inserted through the skin of the midline of the neck, just above the hyoid bone, into the tumor in the base of the tongue. Strange as it may seem, the addition of radon implants in these cases does not appear to increase the local undesirable effects of irradiation to any great extent, but the tumor itself will usually promptly melt away. The use of radon seeds alone in such cases has not been markedly successful, in our experience.

The above described combination of methods also proves useful in the radiation treatment of metastatic cervical nodes. Except in the more anaplastic varieties of intraoral cancer, cervical nodes are not very successfully treated by external irradiation alone. In the metastases from the adult varieties of intraoral cancer, we commonly administer roentgen radiation in divided doses for fourteen to twenty days in dosage sufficient to blister the skin, and immediately after the completion of this treatment, we insert radon seeds, either through skin punctures or after surgical exposure of the outer surface of the node. This combination of methods seems to succeed with fewer undesirable effects than with the use of radon implants alone. Preliminary blistering of the skin by external irradiation is not a contraindication to surgical exposure through the blistered area, if the tissues are handled gently. With proper precautions, healing by primary union invariably takes place.

The same combination of methods is often used in the treatment of primary lesions of the tongue, irradiated first by roentgen rays through the open mouth. It is also useful in small residual tumor masses in the palate or tonsillar region after maximum doses of external radiation. It should be emphasized that the supplementary insertion of radon seeds in the hypopharynx or larynx is sometimes dangerous after heavy external irradiation. In such cases, the procedure is commonly followed by progressive radionecrosis, which is a serious complication in the hypopharynx.

SUMMARY AND CONCLUSIONS

We see no reason why the principle of protracted treatment by radium should not be utilized, either alone or in combination, with roentgen radiation in the treatment of such regions as the breast, uterus, rectum, bladder or in any location where radium therapy has been found advantageous. Modifications in technique would be necessary to meet the problems of the local anatomy and physiology. Most of the protracted radium techniques herein described are intended to be used in conjunction with protracted roentgen irradiation to obviate, at least partially, the disadvantages of the exclusive use of either method alone. We trust that the merits of these techniques will not be judged chiefly in their substitutive and competitive relations to protracted roentgen irradiation. Any unusual qualities of a given remedial agent in the treatment of cancer, whether it be radium, roentgen rays or surgery, are fairly obvious and definite to the unprejudiced and competent observer, who will concede that the best result may often depend on a combination and a complimentary use of two or even of all three of these measures in a given case.

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DISCUSSION

DR. CURTIS F. BURNAM, Baltimore, Md., Dr. Martin and Dr. MacComb have shown us a method of treating certain types of growth. There is, doubtless, a best method of treating each and every growth, but it must vary a great deal, according to the type of growth and, I think, also from individual to individual. Regaud himself has somewhat drawn back from the idea that continuous irradiation is an essential to effectual treatment. The theory is to irradiate when cells are peculiarly susceptible to radiation and there is some reason to believe that this is at the time of nuclear division. However, nuclear division itself is altered by irradiation, and there is no way of definitely determining, in an individual case, when it is at its maximum. Needless to say, clinical experimental work, of the kind that Dr. Martin is conducting, is of very great importance.

Last winter, I had the opportunity of observing some work which was directed toward determining the roentgen dosage necessary to destroy human tumor tissue in culture. This work has been carried out by Dr. George Guy, in Baltimore. Efforts were made to compare the amount of radiation by a single dose, and by a divided dose of equal amounts daily, given over twenty to thirty days. The second method, to produce the same effects, had to be four or five times as great. The impression made upon me is that when tumor tissues are grown in sera, the effects of the irradiation are on the cells and that a very substantial dosage has to be given to destroy them, and that there is a rapid capacity for recovery. On the other hand, it does seem that in the body, there are other agencies which control the effects, and that either antibodies are developed in the sera, or some toxines develop locally, which add to the effects of the irradiation. Of course, this is a conception that has long been held and seems to be clinically evidenced in many cases, but is hard to demonstrate experimentally.

DR. G. FAILLA, New York City. The main question involved here is one of differential recovery. If one tissue recovers more rapidly than another, one may take advantage of the difference in the two rates of recovery in radiation therapy. On the other hand, if all tissues recover at the same rate, nothing is gained by extending the treatment over a period of twenty days or longer. In this connection one should consider also the reaction of the patient's body as a whole and its rate of recovery from radiation effects as compared to the recovery of the local tissues.

It has been shown definitely that skin recovers more rapidly than some tumors and in this lies the advantage of the Coutard method. On the other hand, one should not generalize and assume that *all* tumors should be treated by this method. Thus, supposing that our object was to destroy the skin with little damage to the tumor, it would then be advantageous to administer the radiation in the shortest possible time. It is probable that the recovery rate of some tumors is just as rapid as that of skin, or it may be even more rapid. In both of these hypothetical cases it is preferable to administer the radiation in a short time—provided the body as a whole is not overtaxed. Since treatments extending over a period of weeks complicate the procedure from the point of view of both patient and radiologist, it is important to determine the relative rates of recovery of different tumors and normal tissues, so as to adjust properly and most economically the duration of the treatment for different groups of cases.

DR. LAWRENCE A. POMEROY, Cleveland, Ohio. I would like to ask whether Dr. Martin has used this method in treating tumors of the esophagus. Also what radium dose he has used following roentgen therapy in implantation of tumors of the tongue or the cervical nodes. If he uses 3,500 r does he use the usual 10 S.E.D. or less? Does he cut down the dose of radium in these cases?

DR. HENRY SCHMITZ, Chicago. The principles of the Coutard method are spacing and protraction. Spacing ameliorates radiation sickness and contributes to the safe use of large total doses without causing any increase in the immediate normal tissue reactions. The protraction or long time duration of each seance renders the technique uneconomical, and it is questionable whether long time exposures of one hour are really necessary. From observations made in the institute I feel that they are not necessary.

The five year end-results in carcinomas of the cervix treated with single massive doses, or treated with spaced massive doses or treated with spaced but protracted or slow time doses were practically the same. I wish the men who have had experience with the Coutard method and the other methods would discuss these questions so that we may definitely rule in or

out the necessity of protraction of the spaced or fractionated treatment.

Dr. H. H. Bowing, Rochester, Minn. Dr. Martin is to be complimented on the presentation of a very timely topic. I agree with Dr. Schmitz that we should have liberal discussion concerning fractionation as compared with the continuous dose method. I have been impressed with what the patient can furnish to assist in the healing of his lesion. In treatment with radium, naturally the patient must come into the picture. What he furnishes is something we will probably never be able accurately to determine or fully to estimate. This is a very important phase of our treatment and I do not know that there has been a time in radiation therapy when we have taken it into consideration more than at present.

I am very much interested in spacing, since it is one of the factors which permits us to individualize our therapy. Its application is time consuming and expensive, and it is tedious for the operator, for every time he replaces the applicator it is in a sense a separate treatment and must be done with as much care on each occasion as on the first application. After the second or third observation and treatment the lesion will have changed, the method of attack may be altered, and later, after the final application, there will be a marked change in the lesion and in the patient. The patient feels improved and knows that something has been done, that something is happening within him that is worth while. I regret that there is not enough time for a full presentation of this matter. In the papers we have presented in the conferences on radiological therapeutics at The Mayo Clinic much of the time in treatment has been devoted to the problem of spacing, but I admit as yet it defies analysis.

Dr. Martin (closing). Dr. Pomeroy asked about the use of protracted radium irradiation in cancer of the esophagus. We have used protracted radium irradiation in the esophagus and a discussion of the technique will be included in the published report of the paper just read. It has not been very successful from the standpoint of cure, and probably not as useful as roentgen irradiation in the palliation of esophageal cancer.

Dr. Pomeroy also asked about the dosage of radon seeds which we use for implantation into the tongue after preliminary protracted roentgen therapy. We have no absolute rule for interstitial dosage for these cases since the size of the tumor and the quantity of preliminary roentgen radiation may vary considerably in individual cases. The dosage of seeds in these cases must be more or less empirical, but if the tumor is not too large, one may use a tissue dose up to 10 S.E.D. even after heavy roentgen irradiation. The complication which one would naturally expect, that is, radiation necrosis, does not usually occur since, as we have previously mentioned, it seems that the untoward effects of a combination of two methods are not as cumulative as their beneficial effects.

I am not certain that I have properly understood Dr. Schmitz' question. If he has questioned the value of protracted or fractionated irradiation as compared to massive doses, I can only say that I was under the impression that the principle of protraction or fractionation was rather generally accepted, and I feel that this is hardly the proper occasion to bring up a discussion of this rather complicated question. If he means that the total treatment time, that is, the time which the patient spends under a roentgen-ray machine or under a radium applicator is of less importance than the fractionation of the dosage over a treatment period of from twenty to thirty days, then I agree with him. In our experience, there seems to be little doubt that any type of division of doses, even the division of one dose into but two fractions and giving them on successive days is better than no fractionation at all. As we have already stated in our discussion this morning, we have seen no unusual or remarkable result following continuous irradiation over three or four weeks as compared to interrupted treatments spaced evenly over the same period. This is probably the question to which Dr. Schmitz refers.

Dr. Hauser asked about the dose of radium which can be given after heavy roentgen-ray dosage in recurrences. The answer to this question is practically the same as that given for Dr. Pomeroy's. If recurrences follow heavy protracted external irradiation, any form of radiation given subsequently is attended by the risk of radionecrosis or other untoward effects. However, we believe that such complications occur less frequently or are less severe in degree if the treatment for the recurrence can be given by a different method than that used for the original tumor, as for instance, if one has used roentgen radiation at the beginning, a recurrence which follows this treatment is better treated by radium than by further roentgen irradiation.

EVALUATION OF IRRADIATION IN THE TREATMENT OF UTERINE FIBROIDS*

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WHERE two or more methods of treating a disease or pathological process are of approximately equal value, where each enjoys certain advantages and suffers from certain disadvantages, it is fortunate that practice varies from clinic to clinic, and from doctor to doctor. If it were not for this, progress would be impeded, if not actually stopped. This situation is well exemplified in the problem of selecting the best treatment for uterine fibroids. There are two general methods of treatment: the older is by surgical operation; the newer, but by no means new—it has been used for more than a quarter of a century—is by irradiation either with roentgen rays or radium.

Before actually considering the relative merits of these two methods of treatment, each of which has multiple subdivisions, let me recall some of the more essentially and generally agreed on facts in regard to fibroid tumors of the uterus. These tumors are not malignant, although sarcomatous degeneration does take place in a small percentage of them, and certain women with fibroids do develop cancer of the body of the uterus or of the cervix. It is my opinion that this takes place no oftener than in women who have no fibroids, although there are many statements in the literature to the contrary. Fibroids are much more common after, than before the age of forty. Most of them shrink and a few disappear after the spontaneous menopause. A large number of fibroid tumors of the uterus never give symptoms requiring treatment. They remain small, cause no increase in menstrual bleeding, are painless and do not cause any dysfunction of other organs. Such fibroids should not be treated by operation or by irradiation, or by any other method, except by routine examinations to make sure that the condition is stationary and not progressing. A uterine fibroid condition may be accompanied by pelvic inflammatory disease, sometimes by infection of the fibroid itself. Calcification of the fibroids and cystic changes occur in the larger tumors. The chief indications for treatment in uterine fibroids are those resulting from severe bleeding, such as anemia, and those associated with pressure symptoms on neighboring organs, due to the actual size of the tumor.

In general, a positive diagnosis of fibroids, and of no other condition, can be made. This, however, is much easier where the fibroid is not larger than a three months' pregnancy. In larger tumors, there is a greater proportion of patients in which ovarian and other complications cannot be definitely excluded by any method except an exploratory laparotomy. It is the general opinion of gynecologists, and in this I concur, that irradiation should not be chosen as a method of treatment unless a positive diagnosis can be made without resorting to exploratory laparotomy.

Uterine fibroids are a predisposing cause of sterility, although they do not always prevent pregnancy. It is doubtful how much the sterility is actually relieved by conservative operations, such as myomectomy. In general, the feeling of most gynecologists is that conservative surgery is the method of choice where hope of having a child is the paramount consideration. It is true that uterine fibroids have been treated by irradiation, have disappeared, normal menstruation has returned and subsequent pregnancy developed, and a normal child been delivered. Such a satisfactory result, however, is exceptional and, with our present knowledge of irradiation, impossible to control. Conservative opera-

* Read at the Twenty-first Annual Meeting, American Radium Society, Kansas City, Mo., May 11–12, 1936.

tions and conservative irradiation, aiming to maintain the function of fecundity, are not nearly so likely to be positively curative as more radical procedures. In a large number of these cases, secondary and more radical treatments have to be finally resorted to.

Uterine fibroids, in large measure, owe their growth to substances either secreted by the ovaries or by the effect these substances have on other internal gland activities. It is true that some fibroids persist and even grow after the normal menopause. There are certain clinical observations which support the view that radiation has a direct effect on fibroid tissue, as well as indirectly on the fibroids, through changes produced in the ovaries. It is only necessary to recall that occasionally, by intrauterine radium treatment, a fibroid tumor will disappear without causing cessation of menstruation, and that the recession of fibroids is much greater after the artificial radiation menopause than after the normal menopause. In general, however, it is certain that the principal action is through the effect on the ovaries and that our clinical methods of treatment are directed towards the production of an artificial menopause, either temporary or permanent.

In the early days of radiation treatment of uterine fibroids, we were not sure that we might not do injury to other organs and tissues of the body as a result of treatment. We were uncertain as to whether the treatment might not lead to later malignancy. Experience, I think, has demonstrated that these apprehensions are not justified.

It is not the purpose of this paper to consider in detail the various surgical or irradiation procedures. It is, however, my impression that in patients over forty years old, generally speaking, it is better to produce a permanent artificial menopause; the recurrence of growth and further trouble is so frequent after the production of a temporary menopause. In general, also, external roentgen irradiation affords a more plastic method of treatment, is applicable to more kinds of cases, is less likely to be followed by any sequelae, and is much less trying on the patients than intrauterine radium irradiation. It is obviously much more economical than the external use of large amounts of radium by teleradium procedures.

Excluding, therefore, from consideration all patients under forty years of age where pregnancy is hoped for, excluding all cases where diagnosis is not certain, and excluding all cases associated with complications, what should be the choice of treatment? It is obvious that in large measure the decision will rest with those members of the medical profession who are practicing gynecology.

There is a certain tendency to go in cycles. The present tendency of the American gynecological clinics where both irradiation and operation are employed, is to increase the number of cases treated by surgery and to decrease the number treated by irradiation. One of the most influential considerations leading to this position is the prevalent opinion that the artificial menopause is a condition to be avoided, even at considerable cost. The artificial menopause can be avoided or postponed by surgical procedures which are definitely curative so far as the uterine fibroids are concerned. Reference is made here to hysterectomy with the preservation of the ovaries. The menopause varies as to the time of its onset and as to its duration. There are a good many observers who believe that the menopause begins, on the average, as early as the fortieth year, although there may not be a cessation of menstruation for nearly nine or ten years. In most cases, it is difficult to obtain a definite history which indicates an average duration of more than a year.

It has been experimentally shown in animals, and it has been for a long time observed in human beings, that the artificial menopause produced by the removal of the ovaries, as well as the normal menopause, is accompanied by definite changes in other internal secretory glands and that there are

some changes in metabolism. However, we also know that changes in metabolism occur at different periods of life without any reference to ovarian function. A great deal of added interest to the whole subject has been afforded by the recent advances in endocrinology and the discovery of different substances secreted not only by the ovaries, but by the other internal secretory glands.

It is true that more than 50 per cent of all women who have hysterectomies, with preservation of the ovaries, do have an artificial menopause, in any case, within four years of the operation. It is not known exactly to what this is due, but it has been reported on by a great number of observers. This also has some weight in the question of deciding between a hysterectomy and irradiation to produce an artificial menopause.

The chief advantages of surgery in treating uterine fibroids are that the artificial menopause may be avoided and that a prompt cessation of the bleeding is secured. This is not true if irradiation is employed. Among the disadvantages of operation, as compared to irradiation, might first be mentioned much greater cost and disability. It always means hospitalization of several weeks, the employment of a number of people—doctors, nurses and others—and it is usually followed by a period of a month or more for complete recuperation. This, of course, would not be a deciding factor, but is of importance with the people in the lower economic brackets. The chief disadvantage of surgery in relation to irradiation is its mortality. That this is much greater than with irradiation is beyond any question. It is also true that morbidity is much higher from operations than from irradiation procedures.

The advantages and disadvantages of irradiation can be surmised from what has already been said about operation. It is slower in controlling hemorrhage; it is less definite in doing away with the tumor; it also produces, in the form that is generally accepted to be the best method to use, artificial menopause.

It is difficult to determine what the actual death rate from hysteromyomectomy is. It depends, first, on the skill of the operator and his good fortune in avoiding infection, and, secondly, on the general condition of the patient he is operating on, the size of the tumor and other factors. However, that postoperative death occurs and can never be entirely avoided is obvious. Various statistics on series of 100 or more cases have indicated a death rate of from 1 to 5 per cent. Contrast with this, our experience with 1,800 cases of uterine fibroids treated by irradiation. In this entire group there has not been a single death. Our methods of irradiation today are much safer than those which we employed prior to ten or fifteen years ago.

As a practical guide for conduct, we should always remember, in dealing with patients who have uterine fibroids, that it may be necessary to choose different methods; that some patients should be operated on, that others should be treated by irradiation. For this reason, if no other, it is obviously bad practice to frighten patients as to the possible consequences of either operation or irradiation. Among my patients are some who are greatly afraid of death from operation. We have a great many more who have, either from lay people or from doctors, acquired a most distorted idea as to the bad effects which may arise from the production of an artificial menopause. Such questions are asked as: "Will I be slowed up? Will my vitality be lowered? Will I be permanently anemic? Will I have high blood pressure? Will I pass from youth into old age? Will my mind be affected?" and many other similar interrogations are put which are not worth while repeating.

It is fairly generally conceded now that the results obtained in hemorrhage and in tumors, by methods of irradiation, are satisfactory in properly selected cases. There is, however, a question under lively discussion at present as to whether the escape from the chances of death from operation is desirable when the price re-

quires the assumption of the neurological and psychical disturbances produced by the artificial menopause. Let me say, that all our studies of the past have led us to the impression that the artificial menopause is not a very serious thing from either the physical or psychical standpoints.

It occurred to me that it might be worth while to select a series of 100 consecutive cases treated some years ago, and to study them from the standpoint of results obtained. All of these patients were suffering from uterine hemorrhage. Many of them were markedly anemic. The tumors varied in size from a six months' pregnancy down to tiny fibroids. The average age was forty-four; 83 were married; 17 of the patients were unmarried. Most of the patients were in normal condition, without any other obvious trouble; 3 complained of being excessively nervous before any treatment was given; they were not hyperthyroid cases. Six patients were definitely of the psychic-depressive type, and 2 of these had had definite attacks of depression. Arthritis was present in only one case out of the 100; one case had an associated diabetes; in 7 cases, there was definite hypertension. In none of the patients was a mistake made in diagnosis; all were uncomplicated fibroids. Twenty-eight cases were treated by roentgen irradiation alone, 36 by radium alone, and 36 by combinations of intrauterine and external roentgen irradiation.

Effects on the Tumor. In 59 cases, the tumor has entirely disappeared. In 32 it was reduced tremendously; that is, the tumor was from one-third to one-eighth of the original size. In 8 cases, there was no reduction in the size of the fibroid, but there has been no increase in size over a number of years. In this connection, it is of interest that the complete disappearance of a tumor does not depend on the size of the fibroid. Very large tumors may completely disappear and small ones only partially or not at all. In none of the 9 patients where the tumor was not reduced has there been any necessity for operation, or change indicating any growth or degeneration in these fibroids. During the first years in which we used irradiation, and in which the tumors did not disappear, we did a number of hysterectomies. If a tumor is not causing pressure, or giving any disturbance, an operation is certainly not imperative and further irradiation is of questionable value.

Effects on Bleeding. Bleeding was controlled in all cases, and a complete amenorrhea established. As an immediate result of treatment, there were no marked anemias, no marked changes in differential and total blood counts. The average time for the establishment of the menopause was five and a half weeks, but in some cases it was not obtained for four months.

Arthritis. The one patient with definite arthritis, and who had been under treatment for the arthritis for a long time, showed no change except, perhaps, a slight progress of the disease. This, we do not believe can be attributed to the artificial menopause. There were 9 other patients giving no history of pain or stiffness in the joints before treatment who did develop mild discomforts in the first six months after treatment. The average duration of the trouble was about six months. All were well after a year. No special treatment was given for this condition. It was mainly in the knee and shoulder joints and was thought to be due to some change in metabolism.

Observable Changes in Other Glands. No cases developed any evidence of hypo- or hyperpituitarism, so far as we were able to determine. There were no occipital or other headaches complained of in these patients either before or after treatment. There were no changes in the thyroid gland, although no routine basal metabolic tests were made before and after the establishment of the menopause. As a matter of fact, the effect of the menopause on thyroid activity, as reported in the literature, is very conflicting. So far as I know, we have never had a hyperthyroidism develop after the production of artificial menopause. In one case which I recall, but which was not in this

series and where a definite exacerbation of hyperthyroidism occurred with each menstrual period, there was a very great improvement in the patient by the production of the artificial menopause without any treatment of the thyroid gland.

Effects on Blood Pressure. There is a well-known hypertension associated with the normal menopause and it is frequently described in the literature. It seems to me doubtful that this is actually due to ovarian change; more likely it is a symptom of various changes which take place in advancing life. However this may be, in the 7 cases of definite hypertension that we had in this series, there were no marked changes from the treatment; in fact, nearly all have shown slight reduction in blood pressure. I do not attribute this, however, to the production of the artificial menopause, but to the general care which was given the patients by their physicians for the hypertension. None of the patients with normal blood pressure developed hypertension; there were, in some cases, moderate increases; in others, moderate decreases. Our own feeling is that the menopause has no direct association with the problem of hypertension.

Hot Flushes. Four per cent of the patients presented none whatever; 58 per cent presented quite mild flushes, but they did not worry the patients at all and the fact that they were present had to be elicited by inquiry; 34 had pronounced flushes, associated in most cases with some sweats; 4 cases had quite severe flushes, which gave them considerable discomfort. The average duration of the flushes in all cases was eleven and a half months; the minimum duration was one month and the maximum, three years.

Nervous and Psychic Disturbances. In the 3 patients who complained of nervousness before treatment, it was not relieved, but remained about the same after treatment. Twelve patients complained of nervousness for two or three months; 3 complained for more than a year. No patient complained of very much nervousness, with the exception of one patient who had insomnia. This was present before, but seemed to be worse after the treatment.

In 5 cases of mild depressive conditions, 4 apparently were unchanged by the treatment; one was slightly worse. In 2 patients where there had been definite attacks of depression before treatment, there has been no change for either the worse or the better. There has been no complaint of change in the sexual functions, and there has been no case of dyspareunia as a result of the treatment.

CONCLUSIONS

The production of the artificial menopause does not produce serious or persistent physical or mental changes of any kind. A great many patients volunteer the information that they feel a great deal better after the treatment than they have felt for years. In this connection, it may be recalled that formerly it was frequently observed that when the natural menopause was reached, a great many patients felt in better health, stronger and more active than they had for some years prior to this event. This is, of course, against the normal developments in advancing age. Older persons do not feel better than younger persons, naturally. There is evidence, therefore, that the ablation of the ovarian function may be helpful rather than harmful in the general feeling of well being. It is hardly necessary to refer to the frequent nervous and psychic disturbances of mild character that occur during menstrual life and are directly associated with menstruation. Certainly we have seen no development of the nervous conditions to which some authors refer. In addition to the safety in irradiation to produce the artificial menopause in healthy women, it seems also safe to employ the same measure in psychoneurotics where the local indications for treatment are urgent. It must be remembered, however, that this class, and even normal patients, can be given a great deal of worry if adverse criticism is made of the treatment they have had, or if the physician

himself who is giving the treatment expresses anxiety as to the consequences on the physical or psychic well being of the patients. In none of these patients should treatment be resorted to too hurriedly, and this is particularly true if the patients are depressives. All the effects of the treatment should be fully and considerately explained to the prospective patient. It is well, in addition to obtaining an absolute diagnosis from the gynecologist's standpoint, also to investigate and have a clear conception of the general physical condition, the physical traits and the social surroundings of the patient. Most of the psychoneurotics are referred by psychiatrists and it is certainly wise to advise both the psychiatrist and the patient that the treatment is not directed towards bettering the psychic disturbances, but only to relieve the physical disturbances due to the fibroid, and that any benefit that might occur otherwise would be secondary. For the hot flushes, in most cases, other than reassurance to the patient that they are normal and indicate that the treatment has been sufficient to produce the desired result and that they can look for their disappearance after an interval, no treatment is necessary. If, however, the flushes are very pronounced, it is permissible to resort to ovarian hormone treatment. We personally have had better results from mild irradiation of the hypophysis and the giving of either small doses of iodine or actual thyroid extract. The choice of treatment in any given case of uterine fibroids, provided the patient is forty years or over, should not be influenced greatly by any consideration of the preservation of the ovarian function, but on the basis of the general physical condition of the patient and the actual gynecological findings. These have been fully discussed in many papers and need not be taken up here. Every case should be considered as an individual problem and the tendency to adopt some standard form of procedure for all cases should be sedulously avoided if the problem of what is the best treatment is to be further advanced and the patient is to receive the best treatment which is available for her at this time.

DISCUSSION

Dr. William P. Healy, New York City. I think Dr. Burnam's final sentence summed up the entire subject of his paper and was very well stated.

It may be interesting to briefly review or refer to what I have been doing personally. I was asked to give a little talk on treatment of non-malignant uterine conditions, and in order to find out what I was doing with those cases I took the cases in which we had made a diagnosis of uterine myomata in patients who had passed through my office during 1933 and 1934, inclusive. There were 200 such cases. It was interesting to note that in my opinion two-thirds of these patients would be better treated by surgical procedures and about 65 per cent were advised to have surgical treatment. In the majority subtotal hysterectomy was performed, in some cases complete hysterectomy, and in a few cases myomectomy. The reason for this was that the tumors were large, or in my opinion had complicating conditions or I had suspected there were complicating conditions, so I would hesitate to advise irradiation for them, or there were subperitoneal myomata. The majority of my cases of uterine myomata are under forty years of age and I hesitate to advise in young women enough irradiation for a tumor growth of non-malignant type to bring about an artificial menopause. If the patient is thirty-nine I may not quarrel about it, but if she is in the middle thirties I lean toward surgical procedures. Of the cases not treated surgically 9 per cent were advised that they did not require any treatment. The tumors were small, gave no symptoms, were discovered only in the course of a physical examination, and needed no treatment. The balance were treated by irradiation; in the smaller tumors always by intrauterine radium treatment. In the larger tumors with the patient a poor surgical risk, or anemic from profuse bleeding, or with the tumor as large as a five or six months' gestation, I prefer to combine intrauterine radium irradiation with roentgen therapy. In all cases where the tumor is larger than a three months' gestation I invariably advise roentgen irradiation plus intrauterine radium. I advise this because I wish to be certain of obtaining ovarian cas-

tration. I also invariably advise a diagnostic curettage. I think it is very unwise in a patient over forty years of age in whom we make a diagnosis of tumor of the uterus and the patient has bleeding to treat with roentgen irradiation to terminate the growth of the tumor and to bring about a temporary menopause without a diagnostic curettage being first done. As Dr. Burnam has said, corpus carcinoma is not infrequent as an associated condition with fibromyomata of the uterus, especially when these patients are late in their menstrual life, in the late forties or early fifties, but still having menstrual periods or menorrhagia. It would be very unwise to treat any such cases with external irradiation alone. Even though the patient is a bad risk for a hysterectomy, which you might prefer to do, she should not be treated upon the diagnosis of a benign tumor but with the possibility of a coincident cancer and should have a diagnostic curettage so that if the complicating feature is malignant it may be properly treated. There is no more puzzling problem than the younger patient with a fibroid tumor the size of a two or three months' gestation. She may have one child or no children, and the gynecologists who are using radiation therapy are often unable to tell the patient whether they will treat with irradiation or surgery. This cannot be told until you have done a preliminary curettage, because in many instances you will find only an intramural myoma, and you may decide to use radium to control bleeding, and let the patient go along for a few years with a tumor which may not grow. The patient will not be incapacitated and then when she reaches the middle forties you may proceed in any way you think best. It is a difficult position in which to place the patient as well as the doctor, in these borderline cases, for the patients expect a definite decision before they go to the operating room and it is sometimes embarrassing to say that you will not make a definite decision as to therapeutic procedure until you have made an examination under ether anesthesia.

Dr. Charles L. Martin, Dallas, Texas. It has been my custom to advise surgery for young women with bleeding fibroids but the results have not been entirely satisfactory. If myomas grow as a result of some endocrine dysfunction, as many now believe, a myomectomy does not remove the cause of the trouble and recurrences should be expected. Subtotal hysterectomies are done to avoid the premature menopause which may follow irradiation but I have found, as Dr. Burnam pointed out, that a menopause frequently appears in two or three years after a supracervical operation. I would like to ask him whether he believes that this unhappy result may be avoided by leaving a small amount of endometrium in place when surgery is done. If I understood Dr. Burnam correctly, he states that he obtained relief of hemorrhage in 100 per cent of his fibroid cases. In our own series we have had several cases that continued to bleed after the menopause and in each instance were able to find a submucous fibroid. This lesion does respond well to irradiation.

Dr. Edwin C. Ernst, St. Louis, Mo. In following up our cases we became greatly interested as to the frequency of malignancy in later life. I wonder whether Dr. Burnam has followed that group of cases. I have, fortunately, found very few. Last week we found a case of ovarian carcinoma twelve years after a fibroid operation. In 2 instances through a series of circumstances we were forced to stop treatment and in one case malignancy developed six or seven years later.

Dr. Frank E. Adair, New York City. I would like to ask Dr. Burnam what factors are employed in treating the large fibroid that comes up to the umbilicus.

Dr. Burnam (closing). I did not go into the questions of technique or the general problem of diagnosis, but stated that you must be sure you have a fibroid and nothing else, and that the fibroid is causing symptoms. I agree with Dr. Healy's position entirely that one must be absolutely safe as to diagnosis, and I also mentioned that in some cases we cannot be safe without an exploratory laparotomy, and that it would be better to do a surgical operation if you get that far.

As to Dr. Martin's question, I am not sure that leaving in a little of the endometrium would have any effect on the menopause, in either total or subtotal hysterectomy. It might. We have several cases with that sort of thing, but have not had a sufficient number, or followed them well enough, to draw any definite conclusions. The purpose of my paper was to emphasize that I do not believe it is right to raise the question of artificial menopause

against the radiation treatment of uterine fibroids. Needless to say, there are many cases which are better treated surgically, but for other reasons than the question of artificial menopause.

In the series of 100 cases which I reported, out of a total of 1,800 cases, the techniques I employed were as follows: One-third of the treatments were given by intrauterine radium and roentgen irradiation; one-third by radium irradiation alone; and one-third by roentgen irradiation alone. As the years have gone, we have more and more changed over from intrauterine irradiation to external irradiation. Apparently we get the same results, and there are not the same discomforts and possible dangers. We have seen some cases of carcinoma of the body of the uterus develop in patients who were treated by irradiation for uterine fibroids. It is not clear that there is a definite etiological connection between the two conditions.

As to the method of treating uterine fibroids with roentgen irradiation, we use a 10×20 cm. portal, one front and one back, and, as a rule, divide the treatment into four parts. These can be given on successive days. The actual dosage each day is 500 r with back-scattering. The size of the fibroid, while it adds to the difficulty of accurate diagnosis, does not seem to be very important so far as the results from treatment are concerned. About 60 per cent of the large fibroids disappear after roentgen irradiation, and this same percentage holds for the small ones. So far as bleeding is concerned, we consider a large submucous fibroid as a contraindication to irradiation.

A MODIFIED STANDARD IONIZATION CHAMBER SYSTEM*

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I. THE ROENTGEN, AND THE STANDARD CHAMBER

AIR ionization measurements of roentgen radiations have grown through a sequence of quite similar ideas concerning the unit quantity involved in measuring the radiation. Villard[14] apparently first defined an air ionization unit for quantity of roentgen radiation with his "e," in 1908. This was followed by others such as Duane's "E," an intensity unit,[4] in 1914, and Behnken's "R," a quantity unit,[1] in 1924. All of these units were concerned with the formation of a definite number of ions in 1 cubic centimeter of air under standard conditions. The concept of the single electrostatic unit of charge collected per cubic centimeter of radiated air, a common feature of these previous units, was finally incorporated in the "roentgen" of present general usage.†

The open air chamber provides a means for measuring this unit of roentgen radiation under exactly controlled and reproducible conditions. The development of the chamber has paralleled the evolving concept of the roentgen itself, and many workers are responsible for ideas and refinements in the process of the standard chamber's growth. Among them are Duane,[5] Krönig and Friedrich,[8] Glasser and Portmann,[7] Failla,[6] Küstner,[9] and Taylor.[11,13] At the present time chambers operated with the most careful technique can be made to reproduce the roentgen to within less than 1 per cent error.

† In 1928 the Second International Congress of Radiology in Stockholm[10] adopted the roentgen as an international unit, and defined it, substantially, as follows:

The international unit of roentgen radiation shall be the quantity of roentgen rays which, when the secondary electrons are fully utilized and the wall effect of the chamber is avoided, produce in one cubic centimeter of atmospheric air at 0° C. and 76 cm. mercury pressure, such a degree of conductivity that one electrostatic unit of charge is measured at saturation current. The international unit shall be called the roentgen and shall be designated by the letter r. The effective intensity of the radiation shall be expressed in r per minute, or r per second.

II. A MODIFIED CHAMBER SYSTEM

In the past year an instrument for primary determination of the roentgen to be used in the standardization of air ionization measurements has been constructed and put into operation at the University of Chicago.

The ionization chamber itself is made entirely after the design developed by Taylor and Singer[12,13] at the National Bureau of Standards. It is a guard wire instrument of convenient size, within which ionizing radiations (produced at voltages up to 200 kv.) ionize a definite volume of air as though it were, effectively, freely surrounded by air alone.

The modifications of the system which were felt to be advantageous concern the types of condenser and electrometer used with the chamber and their arrangement in the measuring circuit.

While each of the individual pieces to be described has been employed in other instrument systems, this is the first time in which they are combined for use on the standard chamber.

The condenser, built after a design developed in the Ryerson Physical Laboratory[3] for measurement of cosmic-ray ionization, has two individual cylindrical units between which exists a readily computable standard difference of capacity. This capacity difference, as will be shown, is dependent only upon the difference in length of the two cylindrical units, and, thus constructed, *the two condensers provide within the standard chamber assembly itself an accurate means of determining the collector sys-*

* From the Department of Physics and the Division of Roentgenology, University of Chicago.

tem capacity by ordinary measurements of length and of time.

The electrometer, designed by Dershem,[2] is a small, completely portable quadrant instrument with arrangements for a wide variation of sensitivity. By combining the condenser and electrometer in a single fixed assembly with the ionization chamber (Fig. 1), a rugged instrument is provided, the electrical capacity of which is not altered when the instrument is moved about.

The electrometer has a sensitivity (for this purpose) of about 1 cm. per volt at a scale distance of 50 cm. At this comparatively low electrometer sensitivity, the collector system may be operated so that it is never more than 3 or 4 volts from ground potential. The ionization instrument as a whole will respond readily to low radiation intensities and, with an amber insulated collector system, shows a negligible leakage at these low operating potentials.

Since the condenser and electrometer systems are directly attached to the chamber and are near the incoming beam of radiation, they must be protected with lead shielding. This shielding is shown in Figure 2, which gives a general view of the apparatus. With the aperture of D_3 closed, the standard chamber has a near zero leakage in the direct beam at 200 kv.

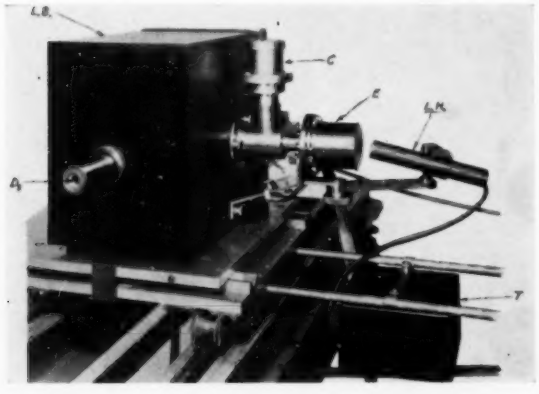

Fig. 1. Standard chamber. *E*, electrometer; *C*, smaller standard condenser; *L.B.*, lead box enclosing ionization chamber; D_3, entrance diaphragm; *T*, transformer for electrometer lamp; *L.H.*, electrometer lamp housing.

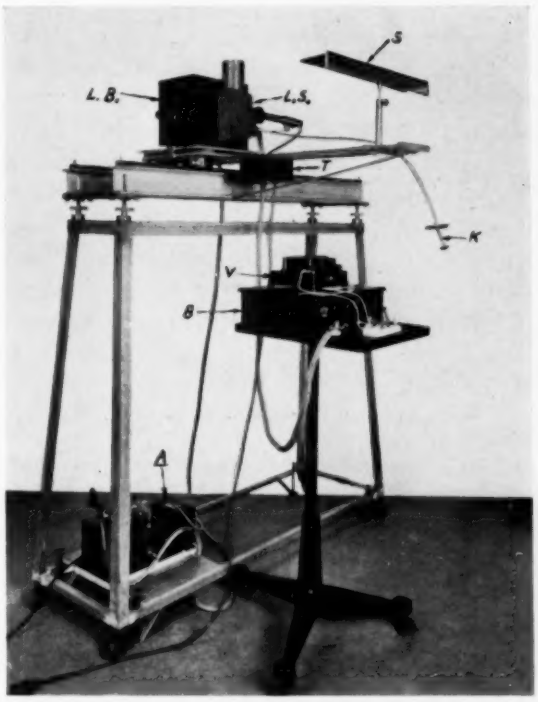

Fig. 2. General view of standard chamber with accessories set up ready for measurement. *L.B.*, lead box enclosing ionization chamber; *L.S.*, lead shield protecting electrometer and standard condenser; *S*, electrometer scale; *K*, electrometer charging switch; *V*, voltmeter; *B*, electrometer battery box with control dials; *T*, transformer for electrometer lamp; *A*, assembly of plate voltage generating and rectifying equipment.

III. Arrangement and Operation of the Chamber System

Figure 3 shows the complete arrangement of the standard chamber system. The lower part of the drawing contains the wiring diagram of the electrometer control and calibrating circuit. B_1 supplies a static potential of about 150 volts to alternate quadrants of the electrometer, *E*. The resistors, R_1, R_2, R_3, permit variation of the potential difference between the electrometer vane and the quadrants, while R_4, with the aid of the split battery circuit, B_2, makes it possible to adjust the collector system (*CP*, *CC*, and the vane of *E*) to ± 8 volts with respect to ground. The voltmeter, *Vm.*, can be switched into the circuit to measure the voltage required to produce a given scale deflection of the

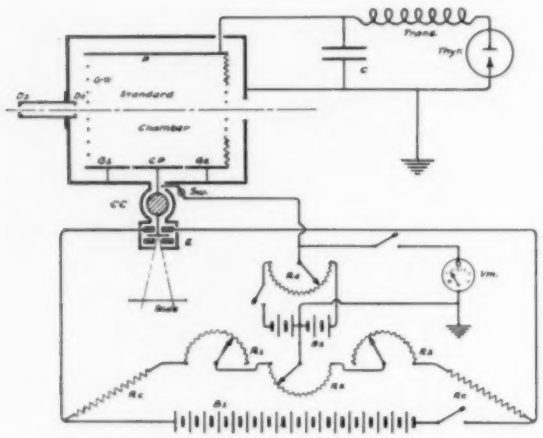

FIG. 3. Diagram of construction of ionization chamber and arrangement of plate and electrometer circuits. Standard condenser at *CC*.

electrometer and to permit a constant check upon the volt sensitivity of that instrument. (In this assembly *Vm.* is a calibrated meter of the Weston Model I type and is actually connected into the circuit with a reversing switch.) The two resistors, *Rc*, are of equal high ohmage and are inserted to minimize the drain on B_1.

Plate *P* of the air chamber is maintained at a stable negative potential of 2,500 volts by means of the transformer and thyratron system, *Trans.* and *Thyr.* A high capacity condenser, *C*, is inserted in parallel with the high tension supply to minimize voltage fluctuations. The potential gradient across the chamber was found to be sufficient to insure saturation conditions of ionization current. The guard wires are shown at *G-W*, with their attendant resistors diagrammed at the right. The wires and the guard plates G_1 and G_2 maintain an effective linear field across the chamber from *P* to *CP*, and thus sharply define the axial limits of the ionized air volume. D_3 defines the diameter of the incoming beam of radiation, and D_4 serves to cut out extraneous radiation. Since the guard plates are grounded, the collector plate is initially set as much above ground potential as it will later be below, due to the incoming negative ions from the ionized volume of air.

In the operation of the instrument, R_4 is adjusted to supply a positive potential of 3 or 4 volts to the charging switch, *Sw.* and thus to the collector system. With *Sw* disconnected, the electrometer is permitted to acquire an equal negative potential while the time interval for the electrometer deflection is observed in seconds with a stop watch.

The intensity of ionization in r per minute is given by the well-known formula:

$$\text{r/min.} = \frac{C \times \Delta V \times 60 \times 760 \times T}{300 \times Vol. \times t \times B \times 273} \qquad (1)$$

where *C* is the capacity in centimeters (e.s.u.); ΔV is the voltage change (in e.m.u.) due to the discharge across to the collector system; *T*, the temperature of the air in degrees Kelvin; *Vol.*, the effective ionized air volume; *t*, the discharge time in seconds; and *B*, the air pressure in millimeters of mercury.

IV. DESCRIPTION AND PRINCIPLE OF THE STANDARDIZING CONDENSER

The type of condenser system used in the apparatus is one which can readily be built

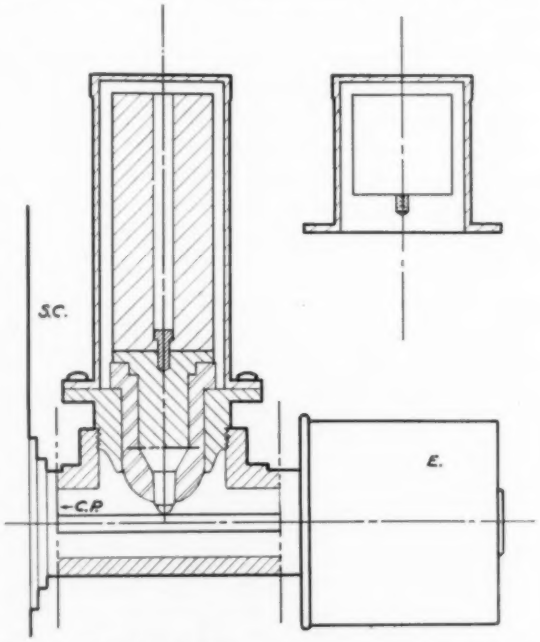

FIG. 4. Standardizing condenser assembly. A schematic cross section (not drawn to scale) showing the arrangement of the concentric cylinders (brass metal designated by single bar, amber insulation by double bar sectioning). *S.C.*, standard chamber; *C.P.*, lead wire from collector plate; *E*, electrometer.

in any good machine shop and which will serve as a standard of capacity difference wherever an ionization chamber is employed—without the necessity of comparison with other condensers.

The capacity determination depends upon the use of two complete condenser units (Fig. 4) each of which is made up of two concentric cylinders: a solid inner one, mounted upon an amber insulating bushing, and a surrounding outer one, at ground potential. The end spacing along the axis between the inner and outer cylinders is identically the same for each of the complete units, while the units themselves differ by a certain definite length. In the apparatus which we have used the inner cylinders are uniformly of 3.175 cm. diameter; the inside diameter of the outer surrounding cylinders is 3.810 cm. The top end spacing, identical for each pair, is about 3 mm. (the exact distance is inconsequential). The height of the inner cylinder in the smaller condenser is 2.540 cm.; in the larger condenser it is 7.620 cm.; and from these dimensions the difference in length of the two units is 5.080 cm.

The capacity of two concentric cylinders can be shown to be:

$$C = K\frac{L}{2\log_e \frac{r_1}{r_2}} \qquad (2)$$

neglecting end effects, where K is the specific inductive capacity of the dielectric (for air $K=1.0$); L, the length of the cylinders in centimeters; and r_1 and r_2, the radii in centimeters of the outer and inner cylinder surfaces. The capacity is then expressed in the electrostatic unit of capacity, the centimeter, which is equivalent to $1.113\mu\,\mu$ f.

If both condensers have the same end spacing between the inner and outer cylinders, their end capacities are identical, and the difference in total capacity between them is:

$$C_1 - C_2 = \frac{L_1 - L_2}{2\log_e \frac{r_1}{r_2}} \qquad (3)$$

in which C_1 is the capacity of the system with larger condenser and C_2 the capacity with the smaller condenser. When each condenser is used alternately in parallel with the collector system, the difference in capacity of the two collector systems is (C_1-C_2). For these condensers (C_1-C_2) is 13.93 cm. It is possible to relate the capacity difference of the two collector systems to the time of charging each to the same potential by means of a uniform ionization current with the following equation:

$$C_2 = (C_1 - C_2)\frac{t_2}{t_1 - t_2} \qquad (4)$$

where t_1 and t_2 are the times of charging corresponding to the capacities C_1 and C_2.

Actual ionization measurements have given the following values:

$$C_2 = 54.4 \text{ cm.}; \quad C_1 = 68.3 \text{ cm.}$$

In making the determination of capacity by ionization discharge, it is essential that the source of radiation be one of constant intensity, or that the measurements be so made and intercompared that a drift in intensity is obviated as a source of error.

V. CALIBRATION OF THIMBLE TYPE INSTRUMENTS

The two thimble type ionometers used in the Division of Roentgenology at the University of Chicago have been compared with the standard chamber by the substitution method[7] under the following two conditions:

Condition Number 1

kv. (peak): 200 Filter: 1.0 mm. Cu
ma.: 25 +1.0 mm. Al
Half-value layer: 1.3 mm. Cu
λ effective (from half-value layer): 0.15 Å

Condition Number 2

kv. (peak): 80 Filter: None (in addition)
ma.: 20
Half-value layer: 2.66 mm. Al
λ effective: 0.37 Å

The tube used in both cases was a General Electric type XPT, having a thick pyrex glass wall with a filtration equivalent of approximately 0.2 mm. Cu. The tube stand itself included a filter of 3.0 mm. of bakelite.

The thimble chamber and the front diaphragm of the standard chamber were alternately inserted at the same point in the roentgen-ray beam. In order that such a procedure might result in significant values[12] it was necessary to have a uniform roentgen-ray beam over the area of the chambers and a steady source of radiation. Validity of the geometrical constants of the volume of ionized air in the standard chamber required a near point source of radiation, and this was obtained by using a very small diaphragm, D_1 (Fig. 5), as the virtual source for the radiations

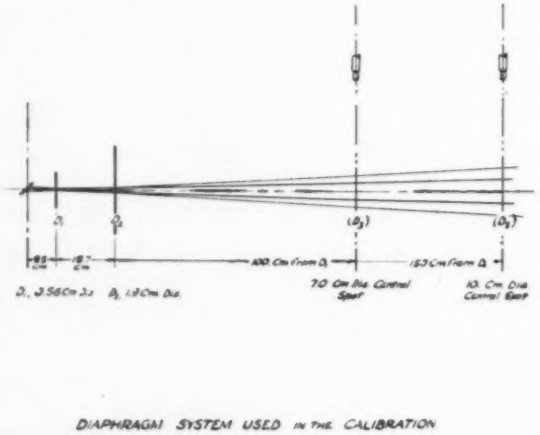

FIG. 5. Diaphragm system between target of roentgen tube and standard ionization chamber. D_1, small diaphragm at port of roentgen tube housing to provide "point source" of radiation; D_2, diaphragm to reduce amount of unwanted radiation; D_3, entrance diaphragm of standard chamber.

coming from the broad focus therapy tube. For condition Number 1, where the tube output was quite constant, the calibration values have an estimated accuracy of 2 per cent. For condition Number 2, where the output was less steady, the accuracy of calibration is estimated to be 4 per cent.

The thimble chambers were found to agree with the standard chamber within a few per cent of their manufacturers' data.

VI. SUMMARY

The developments and improvements in the design of the standard air ionization chamber have gone far toward providing the means for accurately measuring air ionization of roentgen radiations produced at voltages up to 200 kv. In studying various previous forms of this type of apparatus it has been felt that improvement could be effected in the electrical instruments used with the air chamber and also by the manner of their arrangement in the assembly. To this end the usual system was modified by the addition of standard condensers and of an electrometer, all of special design. The arrangement and operation of the modified system are described, and the theory of the standardizing condensers is presented, together with a brief résumé of some calibration measurements made with the apparatus.

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Vol. 37, No. 2

PROTECTIVE FACTORS IN THE PREPARATION AND HANDLING OF GOLD IMPLANTS AND OTHER RADON APPLICATORS*

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THE serious injuries which may result from repeated exposure to relatively weak radioactive radiations are well known. It should therefore be the first requirement where a radon plant is installed to supply adequate protection and instruction for the personnel. This has been difficult in the past, but at the present time proper equipment is available and enough knowledge has accumulated so that there is no excuse for neglect in this respect.

Radon has been used extensively by radiologists since 1914 when Duane introduced the implantation type of therapy in this country. Gradually the methods used in concentrating, measuring, and handling the radon have been improved. Thus the loss of radon has been reduced, the time required for manipulations has been shortened, and the protection to everybody concerned has been greatly increased. Most of these improvements have been initiated and perfected at the Memorial Hospital in New York by Failla and his collaborators. Many of the small emanation plants have, however, not yet been modernized, and no systematic description of all the manipulations has been published. For these reasons we wish to describe briefly the procedures followed, the improvements made, and the apparatus constructed at the University of Minnesota. The apparatus have been built in the University shop at a relatively small cost.

Since the new equipment was installed a considerable quantity of radon has been saved that inevitably would have been lost with the old methods, and the time needed for preparation of the radon has been very much reduced. Though these economical advantages are of great value, they must be considered of secondary importance. The main purpose of the improvements was to secure adequate protection for the technician.

The emanation plant is of the semi-automatic type designed by Failla. The section of apparatus nearest the radium is a continuous source of radiation because it contains appreciable amounts of radon, except for short intervals, and consequently is never free of radioactive deposits. This section is surrounded by 20 mm. of lead which stops the softer radiation and appreciably reduces the intensity of the penetrating gamma rays. Special care should be taken when repair of this portion is carried out and the lead has been removed. The work should be well planned and rapidly performed. The old exposed glass tube should not be held with bare fingers except for a few seconds, if absolutely necessary for the glass blowing. The middle section of the apparatus, where the radon is purified, and the portion where it is collected before being sealed off, contains radon only for shorter intervals amounting to less than one hour daily. These portions, therefore, do not emit considerable amounts of radiation except while filled with radon and for the following two to three hours. During this time the operator should keep away from the apparatus as much as possible, and the automatic pumping arrangement is very helpful in this respect as it makes it possible for him to stay out of the room most of the time while the radon is transferred from one section to the next. We have added as an additional protection against these rays a movable absorption screen which consists of a vertical lead plate 3 mm. thick, 7 feet high, and $3\frac{1}{4}$ feet

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wide, attached to a frame of iron pipes. The frame rests on four wheels and thus the screen can be placed between the plant and the operator when he has to be in the room. He is thus protected from some of the radiations.

We have made one addition to the plant which obviates the concentration of the radon and reduces the time required for the collection, thereby also contributing to minimize the exposure of the operator. It consists of a mercury diffusion high vacuum pump made of pyrex. It is installed as shown in Figure 1. Further description seems unnecessary as the construction of this type of pump is so standardized that anyone familiar with high vacuum technique would have no difficulty in obtaining a satisfactory pump. Our pump was made and installed by the University glass blower. The graded seals soft glass to pyrex had to be added as the emanation plant is made of soft glass. Such seals can be purchased from some of the glass manufacturing firms. We have found this diffusion pump to be useful and time saving. In the first place, before each radon collection the pump evacuates the capillary tubes so well in five minutes that, during a pressure test, no gas bubble can be seen between the mercury and the tip of the glass capillary when a pressure of less than 20 mm. of mercury is used. Previously a piece of the capillary filled with air often had to be sealed off. This waste of time is eliminated. Secondly, the purification section is rapidly and efficiently evacuated after air has been let in for oxidation of the copper gauze or for other reasons. If air accidentally has leaked into the radium solution, it is important to remove it as quickly as possible in order to cut down the loss of radon to a minimum. The diffusion pump is also of value for this procedure by speeding it up

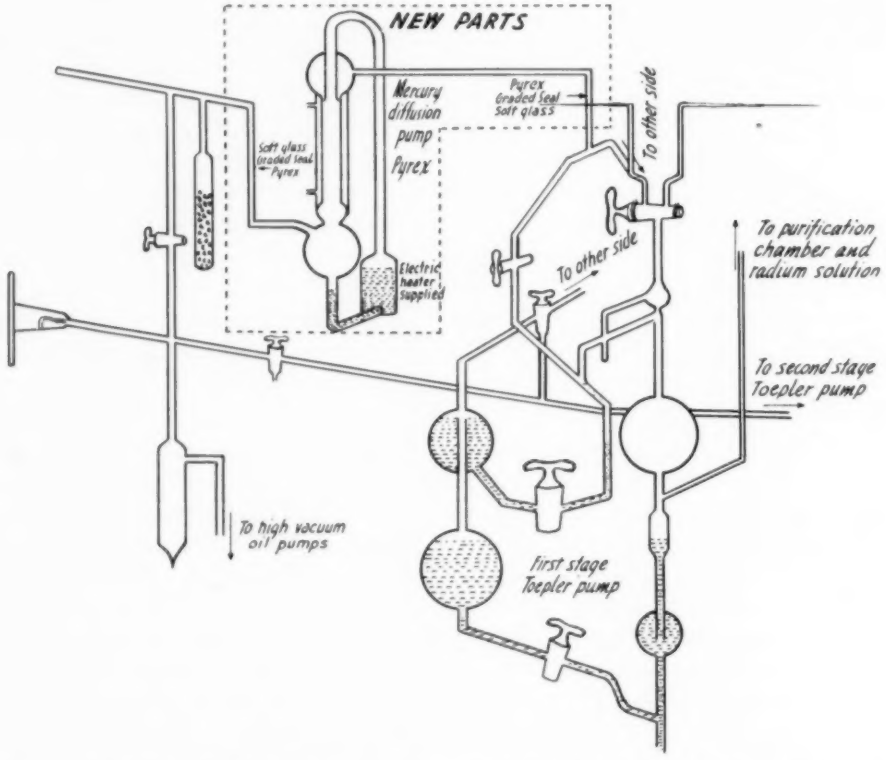

FIG. 1. A section of the radium emanation plant showing the installation of a new mercury diffusion pump.

considerably. The usefulness of the pump is particularly noticed in the making of gold implants. With the higher initial vacuum obtainable, pieces of gold 4 mm. long can easily be filled with 10 to 12 mc. if desired, while formerly 2 or 3 mc. per implant was a maximum.

A manipulation which used to expose the operator unduly was the cutting of gold implants by hand. Such exposure has been almost completely eliminated since the semi-automatic implant cutter was put into use. This rather complicated apparatus, constructed at the University, has recently been described, and the interested reader is referred to the previous publication.[3] A photograph of the implant cutter is shown in Figure 2.

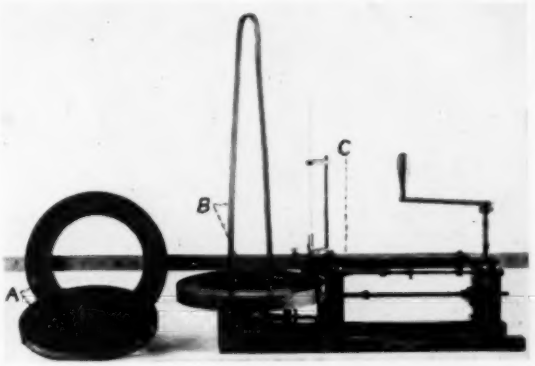

Fig. 2. A semi-automatic gold implant cutter. (For details of its construction see reference 3.) *A*, implant carrier and lead screen; *B*, lead screen and container with long handle attached. A ½ inch vertical lead screen is also used at *C*, but was not present when the photograph was made.

In order to diminish exposure during transportation in the hospital, it is important to have available various lead boxes. Those used for the radium or radon tubes and capsules are simple in construction. We prefer cylindrical containers large enough to hold any of the usual applicators. One of these has an inside diameter of 4.3 cm. and height of 8.5 cm. Both inside and outside walls are made of brass, and between these walls is a layer of lead 2 cm. thick. The top cover also consists of 2 cm. brass covered lead. A removable brass handle 32 cm. long is used when it is carried. This type of handle is used to carry all of our containers. For radium needles, the carriers are constructed in the following manner. Two brass blocks, each about 1×1.5×11 cm., are held together by screws. While thus clamped tightly a series of holes just large enough for the needles has been drilled between the two plates so that half-cylindrical grooves are produced in each plate. By loosening or tightening the screws, it is therefore possible to get a more or less snug fit for the needles. The needles can be threaded while in the holder, and tangling of the different threads is avoided. The brass plates are carried inside of a suitable brass-covered lead box.

Of special importance is the construction of the implant carriers of which we have three types. One is used to collect the implants individually from the implant cutter, to transfer them to the measuring room, and to drop them in the measuring apparatus one at a time. It is cylindrical in shape and consists of two parallel brass plates, each 6 mm. thick and 19.7 cm. in diameter. They are placed together coaxially with the large plane surfaces in contact. At the periphery of a circle of 8.7 cm. radius are fifty symmetrical 6 mm. holes in the upper plate and one such hole in the lower plate. Thus there are forty-nine small pockets in each of which one implant is dropped by the implant cutter while the two plates are rotated together by a special device in this machine. When the carrier is in its proper position on the measuring apparatus, described hereafter, the bottom plate is kept stationary while the top one is rotated in steps. At each step one implant at a time is pushed through the single hole of the bottom plate. The two plates are held together by three small brass ribbons fastened to the lower plate and bent over the edge of the upper. A small vertical hole in the upper plate can easily be lined up with a corresponding hole in the lower and a pin pushed through; thus the plates can be kept locked when desired. The carrier is supplied with a lead cover 7 mm. thick. This is kept sta-

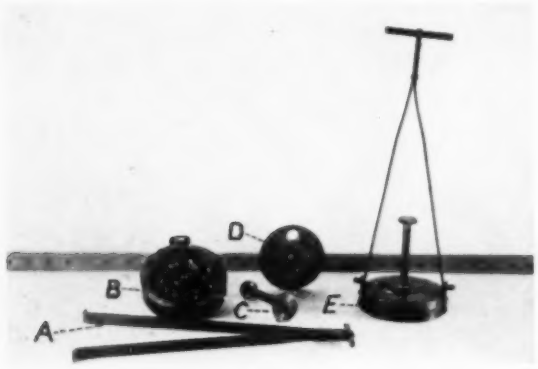

FIG. 3. Radon implant carrier and its various parts: *A*, handle; *B*, lead box with pockets; *C*, key to rotate the lid, and *D*, lead lid; *E*, container assembled.

tionary during the rotation of the carrier and has a small hole through which the implants are dropped into the pockets from the cutter.

The second type of implant carrier is used to collect the implants in groups of equal strength from the measuring apparatus and to serve as a storage box in the supply room. The carrier is made from a lead cylinder 11.8 cm. in diameter and 1.5 cm. high. The bottom is faced with brass, and the top is covered by a 7 mm. lead lid. Fourteen ½ inch pockets are symmetrically cut near the periphery of the cylinder. Small aluminum cups are made to fit into these pockets. Implants are dropped from the measuring apparatus into the cups and may be removed in groups by lifting the cups from the box with long forceps.

The third type of implant carrier is used most often and is handled by the greatest number of people; in it the implants are delivered from the radium department to the places where they are to be used. This carrier is designed to give protection not only to the radium technicians but also to the personnel of the operating rooms. Its special construction facilitates considerably the operating room procedure. The carrier is shown in Figure 3.

The carrier consists of a cylindrical lead plate 10 cm. in diameter and 2.2 cm. thick, with brass covering, and contains six ½ inch pockets into which implants of different strengths may be segregated for the convenience of the surgeon. The pockets are covered by a lead lid 8 mm. thick which is fixed permanently to the box. This permanent feature is new, and has been added since the photograph in Figure 3 was made. When it is desired to remove or put implants into the container, it is necessary to rotate the lid by means of the small outer key until the single hole in the lid comes over a pocket; thus implants can be removed through the hole from one pocket while all other pockets are covered. In the operating room the long handle is removed while the box and implants are immersed in alcohol for sterilization.

Another protective measure is observed by the use of a wagon for hauling the carriers described above to the various rooms. Figure 4 shows the wagon with one-half of the lid opened. The bulk of the wagon consists of a square box 28×28 cm. and 15.5 cm. deep which is large enough to hold every type of carrier used and several of them at the same time. The walls, floor, and lid consist of a central layer of 1.5 cm. thick lead and protective surface layers of 3 mm. chromium plated brass. The box sits on a truck with three wheels equipped with rubber tires and roller bearings. Al-

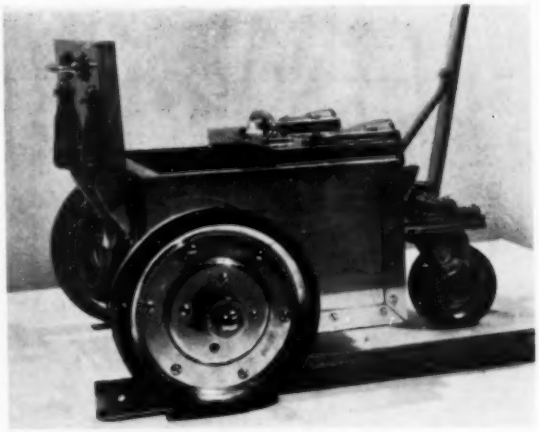

FIG. 4. Lead wagon for the transportation of radium and radon applicators in routine departmental and clinical services.

though the complete wagon weighs nearly 200 pounds, it can be moved with ease, and it runs smoothly and quietly. A long handle can be used either to pull or push the wagon.

Particular precaution against exposure is needed while the individual strength of the radon implants is being measured. This procedure is time consuming when large numbers of implants are handled; moreover, the measurements are usually taken shortly after radioactive equilibrium is established, and at this time the radiation is most intense. The importance of time-saving and protective measures during this procedure is therefore evident. In the old method each implant was picked up by means of forceps, a rather dangerous manipulation; first, because the operator was exposed for a while to the radiation at close range; and secondly, because occasionally an implant would snap from the instrument and fall somewhere in the room. Sometimes it was thus lost or damaged, and became a source of danger until the radon had decayed. Most of these undesirable features of the old method were eliminated by a special apparatus which we have used during the past three years. The increase in protection is accomplished by maintenance of distance between the radon and the operator throughout the process, by lead screening, and by elimination of the use of short forceps. Photographs and mechanical drawings of the new measuring equipment are shown in Figures 5 and 6.

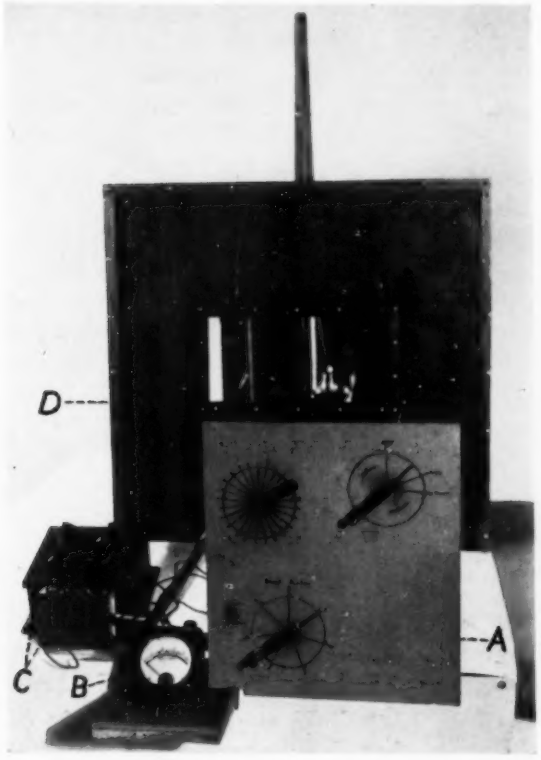

Fig. 5. Front view of apparatus used to measure and sort gold implants. *A*, control board with three control levers; *B*, microammeter; *C*, balancing battery and resistance box; *D*, lead protection screen.

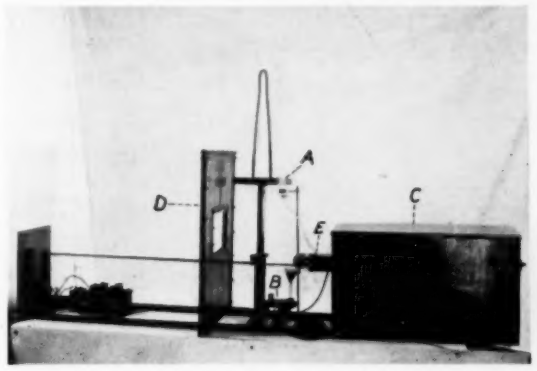

Fig. 6. Side view of measuring apparatus. *A*, implant container from the "cutter"; *B*, storage implant container; *C*, copper box which contains the measuring chamber and amplification device; *D*, lead protection screen; *E*, paper cup on endless belt.

The whole apparatus is placed on a table and rests on a long base made from steel bars. At one end facing the technician is a dial board with three levers by means of which all steps in the manipulation of the implants can be controlled (see Fig. 5). A lateral view of the apparatus is shown in Figure 6. At a distance of 2 feet from the dial board is a $\frac{1}{4}$ inch vertical lead screen equipped with a lead glass window. The implants are kept behind this screen. The large carrier in which they are deposited from the "cutter" is placed on top of a tall brass cylinder (see Fig. 6). Two small rods on top of this cylinder fit snugly into holes in the lower plate of the carrier, keeping

it in a fixed position. A rod contained in the cylinder and extending slightly beyond it in both directions is at the lower end equipped with a beveled gear, and at the upper end with a brass ring. This ring fits in a central hole of the lower plate of the carrier and supports the upper plate to which it is engaged by means of an off-center peg. By moving the left upper lever on the dial board one scale division, the upper carrier plate is turned by means of a connecting rod, the right angle beveled gears, and the vertical rod just enough to push an implant through the peripheral hole on the lower plate. The implant drops through a glass funnel into a small paper cup. Before referring to the next manipulation, a brief description of the measuring device will be given.

A glass cylinder 3.5 cm. high and 6.5 cm. in diameter, with two holes made opposite each other and half way up the wall, is used as the insulating frame of the ionization chamber. Fiber cylinders fit into the top and bottom, and copper plates are fastened to the inside fiber surfaces. The copper plates which form the ionization chamber are parallel and about 1 cm. apart. One plate is electrically connected to the positive side of a 135 volt dry cell battery, and the other plate to the ground through a 0.5 megohm resistance wire. The voltage drop in this wire is amplified with a two-stage amplifier, and the readings are made on a microammeter placed next to the dial board. The ionization chamber is placed inside a heavy cylindrical lead box, the walls of which measure about 2 cm. in thickness. The box is supplied with openings for the leads of the copper plates and also with two holes matching those in the glass cylinder. All of the measuring device except the microammeter, the balancing battery, and a resistance box, is placed inside a large copper box (right in Fig. 6). The lead cylinder with the ionization chamber is mounted on a stand. A small endless belt passes through the chamber, around a wheel, under the lead box, out through the front of the copper box, around another wheel, and back to the chamber. It is on this belt that the little paper cup is mounted in which the implant drops when the left upper lever on the dial board is moved one division.

The next step is to turn the right hand lever on the dial board to a certain point, and the endless belt is thereby moved by means of connecting rods, gears, and wheels so that the paper cup is placed exactly in the center of the ionization chamber. The reading is taken on the meter, and the lever is then turned backwards until the paper cup is tilted enough to drop the implant into a second funnel through which it falls into a pocket of the "storage container." This container is placed below on a disk which can be rotated by means of the left lower lever on the dial board, connecting rods, and gears. All implants of the same strength are dropped into the same pocket. The implants are thus sorted. Each group is then measured together by moving the aluminum cup with long forceps from the lead container to the standard electroscopic measuring device. During the sorting process some ionization in the chamber is caused by the radiation from the outside implants. The zero reading is therefore taken with the implant carriers in position, and it does not change appreciably when the implants are transferred from the upper to the lower container as the distance from the ionization chamber is about the same to both containers.

Occasionally the amount of radiation to which the technician is exposed has been studied by means of a "proteximeter" graduated in tenths of a roentgen. Days have been selected when the amount of exposure was expected to be relatively high. The technician carried the small ionization chamber in a vest pocket. Readings were taken before and after the day's work. The highest exposure in a day has amounted to about 0.1 roentgen. The accuracy of these measurements may be questioned, but they indicate that the protection is adequate for that portion of the body. The fingers receive a somewhat

greater dose but none of the technicians has had any of those changes on the fingertips or nails which have been described as early signs of radiation effects. We therefore believe that the protection is sufficient for departments where the radium supply amounts to less than 1 gram. Where larger quantities are used, similar equipment with some increase of screen thickness and of distances should prove adequate. The relatively simple design of most of the apparatus keeps the cost down so that departments with limited funds can afford them, and certainly the technicians should be protected from all unnecessary hazards.

SUMMARY

1. The personnel who handle radon and radium are inevitably exposed to some gamma and beta radiation. This exposure should be minimized as far as possible. Proper instruction and satisfactory equipment are therefore necessary. A system that has been gradually developed is described.

2. Improvements of the emanation plant consist mainly in an additional diffusion pump.

3. Suitable lead-protected carriers supplied with long removable handles have been constructed for the different types of radium and radon applicators. Three different kinds of implant carriers are used.

4. A semi-automatic implant cutter has added a great deal to the protection of the operator and to the speed of the process.

5. The implants are being measured and sorted in an apparatus designed so that the operator is at an appreciable distance from the implants while manipulating them and is, in addition, shielded by lead. This measuring apparatus contributes a great deal to the safety and to the speed of the manipulation of implants.

6. A wagon is used for transporting the radium and radon containers to different parts of the building. It consists mainly of a heavy lead box so that the containers placed in it are completely surrounded by 1.5 cm. of lead.

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EDITORIAL

MEDICAL USES OF RADIUM

EXPERIMENTS bearing on different phases of radiology are being conducted throughout the world. Unfortunately, the results of some of these experiments are not as well known as they might be, either because the reports appear in publications that are not accessible to the average radiologist or because they are so extensive or so complicated that the average reader has difficulty in obtaining from them the essential information.

Among these numerous experiments attention might be called to a few, the results of which were reported in the Special Report Series No. 204 and 216 of the Medical Research Council of Great Britain, under the title "Medical Uses of Radium." These represent a summary of reports from various British research centers for 1934 and 1935.

It is well known to radiologists interested in therapy that for a number of years attempts have been made to apply the international roentgen to radium therapy. Mayneord, who has devoted considerable attention to this problem, had previously found that at a distance of 1 centimeter from a point source, with filtration of 0.5 mm. platinum, approximately 8.3 roentgens correspond to a milligram-hour. Further work in this direction has tended to confirm Mayneord's previous estimate. Mayneord has also attempted to ascertain the distribution of radium most appropriate for surface applicators. His investigations have led him to conclude that flat, uniform fields of irradiation may sometimes be obtained by distributing radium on flat surfaces parallel to those irradiated. Taking a circular applicator as an example, such a ring of radioactive material "produces a uniform distribution in a plane parallel to the ring at a distance equal to 0.71 of its radius and of roughly the size of the ring. For planes nearer the ring, the intensity at the edge is greater than the intensity at the center. If the distribution near a uniformly distributed disc is considered, for planes close to the disc, the intensity opposite the center is approximately twice that near the edge. It is therefore possible by adding extra radium towards the edge of a uniformly loaded circular applicator to oppose these two effects and obtain an approximately uniform distribution of radiation parallel to any circular applicator." Mayneord has prepared curves to show the amount of radium required on rings and discs for varying sizes of applicator and for varying distances.

Just as interesting and perhaps even more important are the experiments which have been conducted by various workers at the Strangeways Laboratory, at Cambridge. These experiments relate chiefly to the action of radium on cell metabolism. Spear, working with somatic cells in culture, found that a minimum threshold dose is necessary to produce any effect on the cells, and that such an effect is preceded by a latent period. The magnitude of the threshold dose and the duration of the latent period were found to vary according to (1) the type and condition of the cell exposed to irradiation, and (2) the particular biological response selected as a criterion. One of the first effects recognized was a diminution in cell division. After small doses this diminution was followed by recovery to a normal rate of mitosis. Sometimes the diminution in mitosis was compensated by a temporary increase before the normal rate was reëstablished. After larger doses cell division may disappear almost entirely for a time and then strikingly abnormal mitotic figures may be-

come apparent. These, however, are not caused by irradiation only, but may also result from exposure to other injurious agents. Some of the abnormal cells break up and disappear while others complete the process of division but probably die later. Spear also found that the greater the amount of cell division in a culture, the larger the number of degenerating cells seen after exposure. Another interesting finding was that, when measured by the diminution in cell division, the biologic response to gamma radiation is a function of the time and of the intensity factors; when a dose is given in fractions, its effectiveness varies according to the time interval between exposures. A finding of the greatest significance was that "if normal and malignant tissues are cultivated under the same conditions, the same dose of gamma rays causes a greater fall in cell division in the cultures derived from malignant material than in those resulting from normal growth." When rate of growth was taken as a measure of biologic response, larger doses were required to produce measurable effects, and it was found that the latent period following exposure was longer in comparison with that required in the case of cell division. Spears concluded that the effect on rate of growth and on cell division seemed to a large extent to be independent of each other.

Other experiments were conducted on living chick embryos by Hughes, Wilson and Glücksmann, who attempted to determine the relative importance of direct and indirect effects of irradiation. They drew attention to the fact that uneven distribution of radiation throughout the volume of an embryo may produce gross abnormalities or even monstrous forms resulting from the uneven dosage to which the several parts of the chick were exposed. They found that when the whole embryo (in ovo) was irradiated and serial sections prepared, cellular degeneration was most pronounced in those regions where cell division was taking place, but was usually absent from areas where mitosis was not normally found. Small doses had no perceptible effect on the blood vessels, but larger doses caused in the vessels cellular degeneration which was irregular or "regional" in distribution. For this reason, Hughes, Wilson and Glücksmann concluded that such degeneration must be a direct effect of the rays.

Other experiments by Robertson, who used cultures of the protozoon, *Bodo caudatus*, confirmed the observations of the preceding investigators. Certain cells apparently were not immediately affected by irradiation and continued to divide for a short time. This was followed by a definite and increasing check in the production of new cells, with subsequent reappearance of division. The diminished rate of cell division remained lower than normal for a number of hours. The period of greatest check in cell division varied with the part of the curve irradiated and the state of nutrition of the cells, but corresponded to an exposure of between four and eight hours. During the period of greatest check in cellular division, it was found that, after the oldest and largest individual cells of the relatively sensitive group (at the beginning of irradiation) had divided, the cells of the next size group did not enter into division at once, but were apparently forced to grow to a larger size than normal before they could divide. Moreover, this increase in size of the cells was maintained in longer exposures and appeared to be a condition of growth in the presence of radium. Robertson thought this process of temporary morphological and physiological adaptation appeared to permit the resumption of the division rate and might be termed a "radium conditioning" of the cells. As for the sensitive period in the life of the cell, this was found to occupy the time between the end of the first two-fifths of the generation time and some period in the fourth fifth.

Throughout these different experiments carried out by different workers, no evidence of primary or direct stimulation of cell metabolism or growth was found.

Finally, the extensive pathologic obser-

vations made at the Bland Sutton Institute of Pathology at the Middlesex Hospital, London, confirmed the view that the main effect of irradiation is on the tumor cells themselves and not on the vascular supply of the tumor, as has sometimes been claimed. After large doses given over a short period of time, histologic examination shows a considerable degree of vascular change with thrombosis, whereas with small doses or when irradiation is spread over a long period of time the main effect is directly on the cells, and vascular changes are slight or absent. These conclusions are in harmony with the clinical observations of experienced therapeutic radiologists.

A. U. Desjardins

SOCIETY PROCEEDINGS, CORRESPONDENCE AND NEWS ITEMS

Items for this section solicited promptly after the events to which they refer.

MEETINGS OF ROENTGEN SOCIETIES*

UNITED STATES OF AMERICA

AMERICAN ROENTGEN RAY SOCIETY
Secretary, Dr. E. P. Pendergrass, University Hospital, Philadelphia, Pa. Annual Meeting: Chicago, Ill., Sept. 13–17, 1937.

AMERICAN COLLEGE OF RADIOLOGY
Secretary, Dr. B. H. Orndoff, 2561 N. Clark Street, Chicago, Ill. Annual meeting: Atlantic City, N. J., June, 1937.

SECTION ON RADIOLOGY, AMERICAN MEDICAL ASSOCIATION
Secretary, Dr. J. T. Murphy, 421 Michigan St., Toledo, Ohio. Annual meeting: Atlantic City, N. J., June 9–11, 1937.

RADIOLOGICAL SOCIETY OF NORTH AMERICA
Secretary, Dr. D. S. Childs, 607 Medical Arts Bldg., Syracuse, N.Y. Annual meeting: Chicago, Ill., Sept. 13–17, 1937.

RADIOLOGICAL SECTION, BALTIMORE CITY MEDICAL SOCIETY
Secretary, Dr. Howard H. Ashbury, Baltimore. Meets third Tuesday each month, September to May.

RADIOLOGICAL SECTION, CONNECTICUT STATE MEDICAL SOCIETY
Secretary, Dr. Max Climan, 242 Trumbull St., Hartford, Conn. Meets annually in May. Special meetings may be called by the Chairman.

RADIOLOGICAL SECTION, LOS ANGELES COUNTY MEDICAL SOCIETY
Secretary, E. N. Liljedahl, Los Angeles, Calif. Meets on the second Wednesday of each month at the County Society Building.

RADIOLOGICAL SECTION, SOUTHERN MEDICAL ASSOCIATION
Secretary, Dr. Roy G. Giles, Temple, Texas.

BROOKLYN ROENTGEN RAY SOCIETY
Secretary, Dr. E. Mendelson, 120 E. 19th St., Brooklyn, N. Y. Meets monthly on first Tuesday, October to April.

BUFFALO RADIOLOGICAL SOCIETY
Secretary-Treasurer, Dr. Joseph S. Gian-Franceschi, 610 Niagara St., Buffalo, N. Y. Meets second Monday of each month except during summer months, place of meeting selected by the host.

CHICAGO ROENTGEN SOCIETY
Secretary, Dr. R. G. Willy, 1138 N. Leavitt. Meets second Thursday of each month October to May inclusive at the Palmer House.

CINCINNATI RADIOLOGICAL SOCIETY
Secretary, Dr. H. G. Reineke, General Hospital Cincinnati, Ohio. Meets third Monday of each month, October to May, inclusive.

CLEVELAND RADIOLOGICAL SOCIETY
Secretary, Dr. North W. Shetter, 14600 Detroit Ave. Meetings are held at 6:30 P.M. at the Cleveland Chamber of Commerce Club rooms on the fourth Monday of each month from October to April, inclusive.

DENVER RADIOLOGICAL CLUB
Secretary, Dr. K. D. A. Allen, 452 Metropolitan Building, Denver, Colorado. Meets on any month having a fifth Monday.

DETROIT ROENTGEN RAY AND RADIUM SOCIETY
Secretary, Dr. E. R. Witwer, Harper Hospital. Meets monthly on first Thursday from October to May, at Wayne Country Medical Society Building.

FLORIDA STATE RADIOLOGICAL SOCIETY
Secretary, Dr. Harold O. Brown, Tampa, Florida. Meetings held twice a year, May and November.

ILLINOIS RADIOLOGICAL SOCIETY
Secretary, Dr. Cesare Gianturco, 602 W. University Ave., Urbana, Ill. Regular meetings held quarterly.

INDIANA ROENTGEN SOCIETY
Secretary, Dr. C. C. Taylor, Indianapolis, Ind. Meeting held the second Sunday in May annually.

LONG ISLAND RADIOLOGICAL SOCIETY
Secretary, Dr. S. G. Schenck, 115 Eastern Parkway, Brooklyn, N.Y. Meets at Kings County Med. Soc. Bldg. on third Thursday of each month from October to May, at 8:30 P.M.

MICHIGAN ASSOCIATION OF ROENTGENOLOGISTS
Secretary, Dr. C. S. Davenport, St. Lawrence Hospital, Lansing, Mich. Three meetings a year, Fall, Winter, and Spring.

MILWAUKEE ROENTGEN RAY SOCIETY
Secretary, Dr. S. A. Morton, Columbia Hospital, Milwaukee, Wis. Meets monthly. Place of meeting named by the president.

MINNESOTA RADIOLOGICAL SOCIETY
Secretary, Dr. L. G. Rigler, University Hospital, Minneapolis, Minn.

NEBRASKA STATE RADIOLOGICAL SOCIETY
Secretary, Dr. D. A. Dowell, Medical Arts Bldg., Omaha, Nebr. Meets third Wednesday evening of each month.

NEW ENGLAND ROENTGEN RAY SOCIETY
Secretary, Dr. E. C. Vogt, 300 Longwood Ave., Boston, Mass. Meets monthly on third Friday, Boston Medical Library.

RADIOLOGICAL SOCIETY OF NEW JERSEY
Secretary, Dr. P. S. Avery, New Brunswick, N. J. Meets annually at time and place of State Medical Society. Mid-year meetings at place designated by the president.

NEW YORK ROENTGEN SOCIETY
Secretary, Dr. R. W. Lewis, 140 E. 54th St., New York. Meets monthly on third Monday, New York Academy of Medicine, at 8:00 P.M.

NORTH CAROLINA ROENTGEN RAY SOCIETY
Secretary, Dr. Major Fleming, Rocky Mount, N. C. Annual meeting at time and place of State Medical Society. Mid-year scientific meeting at place designated.

CENTRAL NEW YORK ROENTGEN RAY SOCIETY
Secretary, Dr. C. F. Potter, 820 S. Crouse Ave., Syracuse, N. Y. Three meetings a year—January, May, and November.

PACIFIC ROENTGEN CLUB
Secretary, Dr. L. H. Garland, 450 Sutter St., San Francisco, Calif. Meets annually, during meeting of California Medical Association.

PENNSYLVANIA RADIOLOGICAL SOCIETY
Secretary, Dr. L. E. Wurster, Williamsport, Pa. Two day annual meeting will be held Friday and Saturday, May 21 and 22, 1937, Hotel Lawrence, Erie, Pa.

PHILADELPHIA ROENTGEN RAY SOCIETY
Secretary, Dr. B. R. Young, Temple University Hospital. Meeting first Thursday of each month from October to May inclusive, at 8:15 P.M., in Thompson Hall, College of Physicians, 19 S. 22d St.

ROCHESTER ROENTGEN RAY SOCIETY, ROCHESTER, N. Y.
Secretary, Dr. Camp C. Thomas, 476 Lake Ave. Meets on second Thursday from October to May, inclusive, 8 P.M., Rochester Academy of Medicine Building.

ST. LOUIS ROENTGEN RAY SOCIETY
Secretary, Dr. P. C. Schnoebelen, Missouri Bldg., St. Louis, Mo. Meets first week of each month. Time and place of meetings designated by president.

SOUTH CAROLINA X-RAY SOCIETY
Secretary, Dr. R. B. Taft, 105 Rutledge Ave., Charleston. Meets at time and place of South Carolina State Medical Association.

TENNESSEE RADIOLOGICAL SOCIETY
Secretary, Dr. F. B. Bogart, 311 Medical Arts Bldg.

* Secretaries of Societies not here listed are requested to send the necessary information to the Editor.

Chattanooga, Tenn. Meets annually at the time and place of the Tennessee State Medical Association.

Texas Radiological Society
Secretary-Treasurer, Dr. J. H. Smith, Lubbock, Texas
Meets annually one day preceding the meeting of the Texas State Medical Association.

University of Michigan Department of Roentgenology Staff Meeting
Secretary, Dr. C. B. Peirce, University Hospital, Ann Arbor, Mich. Meets each Monday evening from September to June, at 7 P.M. at University Hospital.

University of Wisconsin Radiological Conference
Secretary, Dr. E. A. Pohle, 1300 University Ave., Madison, Wis. Meets every Thursday from 4:00–5:00 P.M., Room 301, Service Memorial Institute.

Virginia Roentgen Ray Club
Secretary, Dr. V. W. Archer, University Hospital, University, Va.
Meets annually in October.

Cuba

Sociedad Cubana de Radiologia y Fisioterapia
Secretary, Dr. Francisco Padron, Enrique, Villuendas 64, Havana, Cuba. Meets monthly in Havana.

British Empire

British Institute of Radiology Incorporated with the Röntgen Society
Meets on the third Thursday of each month, from November to June inclusive, at 8:15 P.M., at 32 Welbeck St., London, W. 1, or as advertised.

Section of Radiology of the Royal Society of Medicine (Confined to Medical Members)
Meets on the third Friday of each month during the winter at 8:15 P.M. at the Royal Society of Medicine, 1, Wimpole St., London, W. 1.

Section of Radiology and Medical Electricity, Australasian Medical Congress
Secretary, Dr. H. M. Cutler, 139 Macquarie St., Sydney, New South Wales.

Radiological Section of the Victorian Branch of the British Medical Association
Secretary, Dr. Keith Hallam, St. George's Hospital, K.E.W., Melbourne, E. 4, Victoria, Australia. Meets monthly from March to Nov. incl. for scientific discussions.

Section on Radiology, Canadian Medical Association
Secretary, Dr. A. H. Rolph, 160 St. George St., Toronto, Ont.

Radiological Section, New Zealand British Medical Association
Secretary, Dr. P. C. Fenwick, The Hospital, Christchurch. Meets annually.

Continental Europe

Belgian Society of Roentgenology
Secretary, Dr. J. Boine, Avenue des Alliés, 134, Louvain (Belgium).
Meets monthly on second Sunday at d'Egmonds Palace, Brussels, except in the summertime.

Sociedad Española de Radiologia y Electrologia
Secretary, Dr. J. Martin-Crespo, Fuencarral, 7, Madrid, Spain. Meets monthly in Madrid.

Société de Radiologie Médicale de France
Meets monthly on second Tuesday, except during months of August and September, 12 Rue de Seine, Paris.

Société Suisse de Radiologie (Schweizerische Röntgen-Gesellschaft)
Secretary for French language, Dr. A. Grosjean, La Chaux de Fonds.
Secretary for German language, Dr. Scheurer, Molzgasse, Biel.
Meets annually in different cities.

Société Francaise d'Electrothérapie et de Radiologie Médicale
Meets monthly on fourth Tuesday, except during months of August and September, 12 Rue de Seine, Paris.

Association of German Roentgenologists and Radiologists in Czecho-Slovakia
Secretary, Dr. Walter Altschul, German University, Prague, II.52.

Deutsche Röntgen-Gesellschaft (Gesellschaft für Röntgenkunde und Strahlenforschung)
Meets annually in April, alternating one year in Berlin, one year in some other German city. Meets in addition every two years with the Gesellschaft deutscher Naturforscher und Aerzte.
Permanent secretary, Professor Dr. Haenisch, Klopstockstrasse 10, Hamburg, Germany.

Süd- und Westdeutsche Röntgengesellschaft
Meets annually in different cities.

Nord- und Ostdeutsche Röntgengesellschaft
Meets annually in different cities.

Dutch Society of Electrology and Roentgenology
Holds two meetings a year in Amsterdam, one in the Spring, and one in the Fall.

Societa Italiana Radiologia Medica
Secretary, Professor M. Ponzio, University of Turin, Turin.

Societatea Romana de Radiologie si Electrologie
Secretary, Dr. G. Gatoschi, Str. Isvor 14–16, Bucarest.
Meets second Monday in every month with the exception of July and August.

All-Russian Roentgen Ray Association, Leningrad, USSR in the State Institute of Roentgenology and Radiology, 6 Roentgen St.
Secretaries, Drs. S. A. Reinberg and S. G. Simonson.
Meets annually.

Leningrad Roentgen Ray Society
Secretaries, Drs. S. G. Simonson and G. A. Gusterin.
Meets monthly, first Monday at 8 o'clock State Institute of Roentgenology and Radiology, Leningrad.

Moscow Roentgen Ray Society
Secretaries, Drs. L. L. Holst, A. W. Ssamygin and S. T. Konobejevsky.
Meets monthly on the first Monday at 8 o'clock, the place of meeting being selected by the Society.

Polish Society of Radiology
Secretary, Dr. Jan. Kochanowski, 45 Gornoslazka St., Warsaw. Meets annually.

Warsaw Section, Polish Society of Radiology
Secretary, Dr. B. Krynski, 11 Zielna St.
Meets once a month except in the summertime.

Scandinavian Roentgen Societies
The Scandinavian roentgen societies have formed a joint association called the Northern Association for Medical Radiology, meeting every second year in the different countries belonging to the Association. Each of the following societies, with exception of the Denmark Society, meets every second month except in the summertime.

Society of Medical Radiology in Sweden
Meets in Stockholm.

Society of Medical Radiology in Norway
Meets in Oslo.

Society of Medical Radiology in Denmark
Secretary, Dr. G. Biering, Copenhagen.
Meets on the second Wednesday of each month from October to July in Copenhagen, at 8 o'clock in the State Institute of Roentgenology.

Society of Medical Radiology in Finland
Meets in Helsingfors.

Vienna Roentgen Society
Meets first Wednesday of each month, at 6.30 P.M. at Zentral-Röntgen Institut des allgemeinen Krankenhauses Alserstrasse 4.

Orient

Japan X-Ray Association
c/o Orthopedic Surgery, Tokyo Imperial University.
Meets annually in April.

Kinki Roentgen-Abend Society
Director, Dr. Prof. Taiga Saito, Ogawaoike Tyoto Japan. Meets bi-monthly on third Sunday.

BOOK REVIEWS

Books Received Are Acknowledged under Heading: Books Received. This must be regarded as a sufficient return for the courtesy of the sender. Selections will be made for review in the interests of our readers as space permits.

MORPHOLOGISCHE UND TIEREXPERIMENTELLE STUDIEN ÜBER DAS SCHLEIMHAUTRELIEF DES MAGEN-DARMKANALS. Beitrag zur Kenntnis der anatomischen Unterlage des Schleimhautreliefs und des Mechanismus der Faltenbildung. (*Acta radiol.*, Suppl. XXXI.) Von Sten Grettve. Aus der Röntgenabteilung (Prof. Gösta Forssell) und der anatomischen Abteilung (Prof. Carl Hesser) des Karolinischen Instituts zu Stockholm. Paper. Price, Swed. cr. 10:—Pp. 124, with 43 illustrations. Stockholm: P. A. Norstedt & Söner, 1936.

From an extensive series of experimental, pharmacologic and morphologic studies the author supports the conception of Forssell that there is autoplasia of the mucosa and that changes in this autoplasia produces variations in the mucosal relief. As was established by Dyes and others previously in the case of the human gastric mucosa, the normal relief undergoes marked physiologic variations depending on the physiologic demands upon the stomach. All these investigations point to the fact that the mucosal folds are physiologic rather than anatomic structures and are dependent on the tonus of the muscularis propria and on the autoplasia of the muscularis mucosa and that they are not preformed structures in the sense that Chaoul regards them. The author's investigations are important, especially in regard to the diagnosis of diseases of the gastrointestinal tract through study of its relief and particularly where inflammatory lesions are suspected.

A. ANGSPRENGER

UROLOGICAL ROENTGENOLOGY: A MANUAL FOR STUDENTS AND PRACTITIONERS. By Miley B. Wesson, M.D., Ex-President American Urological Association, and Howard E. Ruggles, M. D., Roentgenologist to University of California Hospital, St. Luke's Hospital, and Clinical Professor of Roentgenology, University of California Medical School. Cloth. Price $5.00. Pp. 269, with 227 illustrations. Philadelphia: Lea and Febiger, 1936.

The arrangement of text and illustrative material in a form to permit ease of reading and ready reference is most pleasing in this new survey of urologic roentgenology. The authors and publisher are to be complimented on the illustrations which are entirely in the negative phase. These should make the book more useful to both student and physician.

The authors have presented in considerable degree, and yet tersely, the pertinent clinical features of disease of the urinary tract, correlating the roentgen pathology with these data. The bibliography has been well selected.

The inclusion of some consideration of cystourethrograms in the diagnosis of disturbances of the lower urinary tract brings up to the present time the important developments in methods of examination. The only major diagnostic criterium omitted has been the comparative reaction of hypernephroma and papillary carcinoma to roentgen therapy. The advantages and disadvantages of retrograde and excretory pyelography together with the various other methods of examination have been carefully and fairly presented.

This book should be a valuable part of the library of the student in the clinical years of medical school and of the general physician as well as the urologist and the roentgenologist.

CARLETON B. PEIRCE

L'ARTÉRIOGRAPHIE DES MEMBRES ET DE L'AORTE ABDOMINALE. ETUDE CRITIQUE. Par Henri Reboul, Ancien Interne des Hopitaux de Paris. Paper. Price, 40 fr. Pp. 137, with 82 illustrations. Paris: Masson et Cie, 1935.

Reboul sketches briefly the history of the development of arteriography and adds the account of his own experience which led him to favor abrodil and tenebril as the best opaque media. The disadvantages of these substances are few, and mainly due to their irritative, yet avoidable effect on the nerves. At present it is difficult to estimate the quantity of medium necessary for the best visualization of the vessels in a given case. The vasomotor stability of the patient is of greatest importance in carrying out the test which seems to be contraindicated in all patients who show vasomotor reactions. The injection of the opaque medium

is carried out by means of a special instrument which accurately controls the quantity and the pressure of the opaque solution. The author presents eighty-two illustrations, first, of the normal vascular tree, and then of pathologic processes in the vessels. He feels that the few disadvantages of arteriography are counterbalanced by its advantages as a diagnostic procedure. It permits an exact diagnosis of arterial obliteration and at the same time it demonstrates the status of the collateral circulation in conditions such as embolus, arteritis and renal or osseous tumors. Most important are the therapeutic indications furnished by angiography, especially in cases of gangrene. Reboul feels that with further refinement of technique and with more experience, the method will develop into a most valuable way to study the vascular system. The excellent textual presentation of this study is supplemented by a bibliography of the important works on the roentgenography of the blood vessels. This monograph is invaluable to those whose interest lies in any of the fields where the study of the blood vessels is important.

E. T. Leddy

Radiothérapie gynécologique: Curie- et roentgenthérapie. Par R. Mathey-Cornat, Radiologiste des Hôpitaux. Médecin de la Fondation Bergonié (Centre anticancéreux de Bordeaux et du Sud-Ouest). Chef du Service central d'Electroradiologie des Hôpitaux du Groupe Pellegrin-Le Tondu. Paper. Price, 60 fr. Pp. 370, with 81 illustrations. Paris: Masson et Cie, 1936.

As the author mentions in the introduction, the extension of radiotherapy during the last fifteen years has been surprising. This book is an attempt to set forth the present status of radiotherapy for gynecologic diseases and disturbances in general. It is printed on good paper, the material is well arranged, and the limited number of illustrations have been chosen to show what they are supposed to show. The first part (three chapters) deals with the biologic foundation of radiotherapy, technique in general, and clinical data concerning benign tumors and conditions as affected by radiotherapy. The second part (five chapters) deals with uterine adenomyomas, endometriosis and endometrioma, uterine fibromyoma, benign menorrhagia or metrorrhagia, sterilization by means of radium or roentgen rays, and the question of radiotherapy during pregnancy. The third part (five short chapters) deals with glandular radiotherapy, disturbances of menstruation, ovarian insufficiency and menopausal disturbances, sterility, dysmenorrhea and other genital neuralgias. The fourth part (four chapters) covers vulvo-vaginal diseases, recto- or vesicovaginal fistula, vaginal prolapse of the uterus, metritis and cervicitis. The fifth part (two chapters) is devoted to general inflammatory conditions of the genital structures and to tuberculosis of the uterus and adnexa. The sixth part (four chapters) covers malignant tumors of the vulva, malignant tumors of the vagina, malignant tumors of the uterus, and malignant tumors of the adnexa, including the ovaries. The seventh part is devoted largely to cancer of the breast, but partly to carcinomatous mastitis, sarcoma or other cutaneous tumors of the breast, as well as to benign and inflammatory conditions of the breast.

On the whole, this is an excellent book which represents a thorough discussion of the many different phases of the subject. In general, the opinions expressed are sound and are based on adequate grounds which are clearly set forth. The second half of the book, dealing with malignant tumors, is perhaps slightly superior to the first part which deals mainly with benign and inflammatory conditions. In the latter portion an occasional inaccuracy has been allowed to creep in. For instance, the author credits Heidenhain and Fried with being the first to use roentgen rays for inflammatory processes. The author apparently subscribes to the idea that roentgen rays or radium may directly stimulate cellular activity and also the idea that the favorable effect of the rays on certain conditions may be explained by direct action on the sympathetic nerves. The Arndt-Schultz law is also mentioned as if it were generally accepted. With these few exceptions, the book is to be commended as a fair and thorough appraisal of radiotherapy in the field of study. While some references to work done outside of continental Europe are included, it may be said to represent more strictly the work of the French, German and Italian schools, with emphasis on the first. Radiologists and gynecologists who wish to keep abreast of the present trends in gynecology, especially with reference to continental European methods, will find this a most useful work.

A. U. Desjardins

RADIUMDOSIMETRIE: VERFAHREN UND BISHERIGE ERGEBNISSE. (*Fortschr. a. d. Geb. d. Röntgenstrahlen*, Ergänzungsband 49.) Von Dr. Karl G. Zimmer, Assistent an der Strahlenabteilung des Cecilienhauses, Berlin-Charlottenburg. Mit einem Vorwort von Priv.-Doz. Dr. A. Pickham, Direktor des Cecilienhauses. Paper. Price, M. 6.50. Pp. 40, with 33 illustrations. Leipzig: Georg Thieme, 1936.

In this booklet Zimmer summarizes more for the physicist than for the physician the latest works on the subject of radium dosage. The question is taken up under two heads, first the determination of radiation in and around applicators, and second the determination of an absolute dosage unit—the roentgen. The various methods of dosimetry are discussed with special emphasis on ionization measurements with biologic control. Alpha and beta radiation, telecurietherapy and protective measures are also considered. A list of seventy-eight references closes the monograph.

Although many therapists will regard this book as a bit "highbrow," Zimmer deserves great credit for this attempt to simplify what is still a highly complicated and technical subject.

E. T. LEDDY

L'ANNÉE ÉLECTRO-RADIOLOGIQUE. Deuxième Année (1934–1935). Par Morel-Kahn, avec la collaboration de MM. G. Appell-Duclaux, L. Babaiantz, P.-H. Codet, R. Coliez, A. Devois, T. Fainsilber, H. Fischgold, G. Gauducheau, P. Guilhem, P. Marquès, Nemours-Auguste, R. Savignac, E. Speder, W. Strouzer, L. Stuhl. Paper. Price, 40 fr. Pp. 266, with 38 illustrations. Paris: Masson et Cie, 1936.

The second issue of "The years in electroradiology," like the first, consists of chapters by French authorities on those subjects which are of greatest interest or importance in keeping the French internist, surgeon or general practitioner up to date on the developments in electroradiology. As before, the book is in four parts, diagnostic radiology, general radiotherapy, electrology and reports of various meetings. The material is well and briefly presented but many of the roentgenograms suffer from poor reproduction. The book appeals to those interested in radiology rather than to those who specialize in it.

E. T. LEDDY

BOOKS RECEIVED

THE 1936 YEAR BOOK OF RADIOLOGY. Diagnosis: Edited by Charles A. Waters, M.D., Associate in Roentgenology, Johns Hopkins University; Assistant Visiting Roentgenologist, Johns Hopkins Hospital; Associate Editor: Whitmer B. Firor, M.D., Assistant in Roentgenology, Johns Hopkins University; Assistant in Roentgenology, Johns Hopkins Hospital. Therapeutics: Edited by Ira I. Kaplan, B.Sc., M.D., Director, Division of Cancer, Department of Hospitals, City of New York; Director, Radiation Therapy Department, Bellevue Hospital, New York City, etc. Cloth. Price, $4.50. Pp. 604, with 616 illustrations. Chicago: The Year Book Publishers, Inc., 1936.

ROENTGEN INTERPRETATION: A MANUAL FOR STUDENTS AND PRACTITIONERS. By George W. Holmes, M.D., Roentgenologist to the Massachusetts General Hospital and Clinical Professor of Roentgenology, Harvard Medical School, and Howard E. Ruggles, M.D., Roentgenologist to the University of California Hospital and Clinical Professor of Roentgenology, University of California Medical School. Fifth edition, thoroughly revised. Cloth. Price, $5.00. Pp. 356, with 243 illustrations. Philadelphia: Lea and Febiger, 1936.

ROENTGENOGRAPHIC TECHNIQUE: A MANUAL FOR PHYSICIANS, STUDENTS AND TECHNICIANS. By Darmon Artelle Rhinehart, A.M., M.D., F.A.C.R., Professor of Roentgenology and Applied Anatomy, School of Medicine, University of Arkansas; Roentgenologist to St. Vincent's Infirmary, Baptist State Hospital, etc. Second edition, thoroughly revised. Cloth. Price, $5.50. Pp. 431, with 183 illustrations. Philadelphia: Lea and Febiger, 1936.

ROENTGENKIMOGRAFÍA CONCÉNTRICA. Por Alberto C. Morelli, Instituto de Radiologia de la F. de Medicina de Montevideo. Paper. Pp. 34, with many illustrations. Montevideo: 1936.

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DEPARTMENT OF TECHNIQUE

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A SIMPLE TECHNIQUE FOR INTRAVAGINAL ROENTGEN THERAPY*

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THERE are obvious advantages in treating malignant lesions of the vagina and cervix uteri by applying the roentgen rays directly to the part treated. I employed and reported[1] such a technique in 1921. However, it was abandoned because of the hazards associated with the use of unprotected tubes and high tension leads. The advent of shock-proof apparatus has made it possible to treat intravaginal lesions without danger and without complicated maneuvers.

Fig. 1. Reproduction of photograph describing intravaginal radiation technique published in 1921.

There are but three items necessary in order to employ this technique:

1. A metal cone measuring 14 cm. in length with an outlet 4 cm. in diameter. This cone fastens to the shock-proof casing in the conventional manner.

Fig. 2. Showing glass specula with the rubber bulb partially inflated, and metal cone.

2. Two glass vaginal specula, made from Paramount urine specimen bottles which are carried in stock by the hospital and supplied to the wards. They are cut in two lengths, 7.5 and 13 cm. respectively. They taper slightly from 5 to 4.5 cm. Being made of cheap glass they contain considerable lead and have a filter value about equal to 0.5 mm. sheet lead.

3. A small rubber composition bag with a two-way inflating bulb.

The glass speculum, either long or short, as indicated, is employed in subjects when there is no difficulty encountered in inserting a large instrument. In other more difficult subjects when there is bleeding, a nar-

[1] Merritt, E. A. Possibilities of intra-vaginal x-ray therapy with description of technique. *J. Radiol.*, 1921, *2*, 29–34.

* From the Radiological Clinic of Drs. Groover, Christie and Merritt.

row vagina or a small introitus, the rubber bag is used. This is inserted deflated into any vagina without difficulty and is then inflated to the threshold of discomfort. On separating the labia the inflated bag presents at the introitus; naturally the vaginal walls, including the bladder and rectum, have been displaced by the distended bag while the vaginal sphincter prevents its complete extrusion.

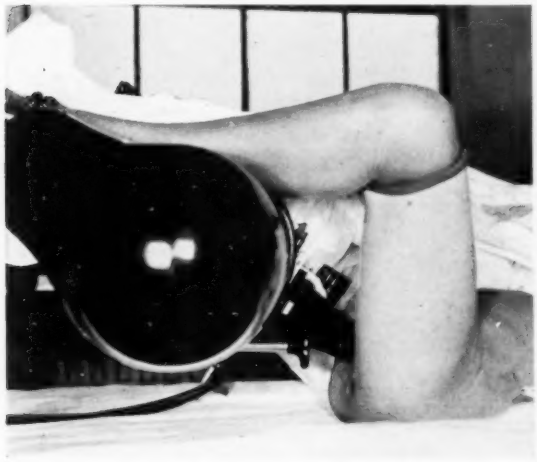

Fig. 3. Patient postured for treatment when using either cone or the bag.

In posturing, the patient's legs are extended over the tube housing and the cone inserted either in the large end of the glass speculum or against the distended bag, with the labia retracted to permit of perfect coaptation between bag and cone. The glass speculum permits of somewhat more accurate focusing of the beam on the lesion, but this is more theoretical than practical.

The focal-lesion distance is 30 and 33 cm. respectively when using the short or long speculum. When the composition rubber bag is used the distance to the lesion is about the same as when using the short speculum. The diameter of the irradiated field is 3.5 cm. with the glass speculum and with the bag the field is approximately 5 cm.

The question of dosage is governed by the same regulation prevailing under identical conditions in other parts. It is apparent, of course, that the short focal-lesion distance permits of a comparatively high intensity of radiation so that when using a filter equivalent to 2 mm. copper the time factor is correspondingly brief.[2]

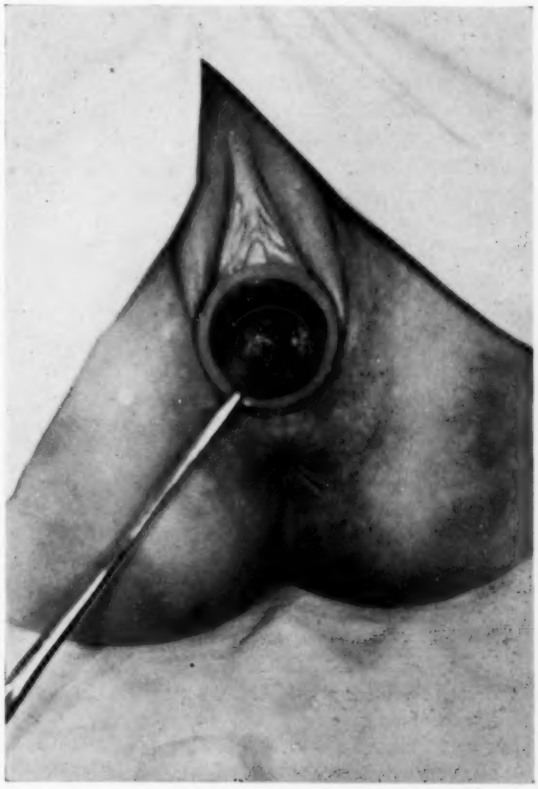

Fig. 4. Speculum in position exposing malignant lesion involving the cervix.

[2] Further experience with the speculum has shown that a hard, rubber speculum with approximately the same measurements is more satisfactory and increases the diameter of the intravaginal field, and further, that the effect on the vaginal wall by the divergence of the beam is of no consequence.

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ABSTRACTS OF ROENTGEN AND RADIUM LITERATURE

ROENTGEN DIAGNOSIS

SKELETAL SYSTEM

Lönnerblad, Lars. Über zwei seltene anomalien (?) im Carpus. (Two unusual anomalies in the wrist.) *Acta radiol.*, 1935, *16*, 682–690.

Three cases are described in which the semilunar and cuneiform bones were fused into a single bone and one in which the trapezoid and os magnum were fused. These were the only abnormalities in the skeleton and there was no evidence of similar abnormalities in the families of the subjects.

Fusion of the whole wrist or ankle into a single block has been described in quite a large number of cases. These anomalies were congenital. But only a few cases of two wrist bones alone have been described. Fusion between the cuneiform and semilunear is the most frequent. Twenty-eight cases of this are collected from the literature. It is not certain whether the fusion in the author's cases was a congenital anomaly or due to some pathological process, though he thinks the former more probable. It would be very unusual for inflammation to cause a fusion between only two wrist bones, as the joints between the carpal bones communicate with each other and are practically never infected alone. There is no explanation for the fact that the semilunar and cuneiform are the bones most frequently fused. The anomaly does not cause any pain or limitation of movement. There is no special change of structure of the fused bones.—*Audrey G. Morgan.*

Dentici, Lorenzo. Osso scafoide accessorio bilaterale. (Bilateral accessory scaphoid bone.) *Radiol. med.*, 1935, *22*, 1010–1012.

The author describes a case in a girl of thirteen who came for treatment on account of pain, swelling and redness on the inner border of the left foot. Roentgen examination showed an accessory scaphoid bone. A roentgenogram of the other foot was then taken and a similar bone found there.

Some authors have held that accessory scaphoid bones are caused by detachment of the tuberosity of the bone but others hold that they are true sesamoid bones in the terminal part of the tendon. It is certain that an independent scaphoid cartilage is found in the human embryo at the age of two months and probably an accessory bone in the adult is due to lack of fusion taking place between this and the main body of the bone. In some animals there is an accessory scaphoid, while in others it exists only during fetal life and becomes united with the rest of the bone after birth.

An accessory scaphoid may cause pain and limitation of function. It is almost always bilateral and this serves as a point of differentiation from fracture. The only method of diagnosis is by roentgen examination. In the author's case he thinks the pain and swelling may have been caused by rapid development of the accessory bone at puberty, independent of trauma or even of pressure by the shoe.—*Audrey G. Morgan.*

Porro, N. L'emangioma vertebrale. (Vertebral hemangioma.) *Arch. di radiol.*, 1935, *11*, 143.

The author describes a case in a girl aged twenty-six. Her illness had begun in 1928 with weakness of the legs. Within three months she could not stand and was obliged to go to bed. On medical and roentgen examination a diagnosis of Pott's disease was made and she was bedridden for years. She was treated at various hospitals and finally sent to the author as a case of chronic Pott's disease. Roentgen examination did not show the picture of Pott's disease but showed a lesion limited to the 5th dorsal vertebra. This vertebra was relatively transparent and the shadow was not homogeneous. There was a central clear area which was trabeculated. There were dense vertical parallel shadows running through the body of the vertebra. These vertical shadows are very characteristic, even pathognomonic of hemangioma of the vertebrae.

The long course of the disease, eight years in this case, is not unusual. Very few cases of hemangioma of the vertebrae have been reported in the literature; this is the 34th that the author knows of. But this form of tumor is found frequently on autopsy. This discrepancy is explained by the fact that there are two groups of these tumors. Those of the first group are large enough to cause compression of the

cord and give clinical pictures such as that described here, while those of the second group are simply dilatations of the vessels in the body of the vertebrae and may cause no symptoms at all. The first kind are usually seen in young persons, the second in elderly persons.

Decompressive laminectomy may be performed in these cases but it is dangerous because of the copious hemorrhage that may occur. It has been performed in 10 cases with a mortality of 60 per cent. Radiotherapy has been tried and in some cases with success as hemangiomas are rather radiosensitive. The author is trying roentgen therapy in his case; if it does not prove effective after a reasonable time he will recommend operation as otherwise the compression will eventually prove fatal.—*Audrey G. Morgan.*

Stewart, T. D. Spondylolisthesis with separate neural arch (pseudospondylolisthesis of Junghanns). *J. Bone & Joint Surg.*, July, 1935, *17*, 640–648.

Author's summary: "In a collection of Eskimo and Indian skeletons, three specimens were found with first degree or second degree spondylolisthesis without separate neural arch. The type of vertebral displacement is shown to be due to arthritic erosion of the articular facets and, therefore, identical with the so-called 'pseudospondylolisthesis' of Junghanns. Because of the infrequency of this condition, a large series of adult spines of these racial groups has been studied with the aim of detecting possible etiological factors.

"On the basis of the usual distribution of lipping of the vertebral bodies, it is pointed out that displacement is apparently not responsible for the lipping in the present cases. A study of the distribution of arthritic facets shows that other regions of the column may be more frequently involved than the lumbar. Within the lumbar region the frequency favors the fourth and fifth lumbar joint and the female sex. The locations of arthritic facets suggest that trauma connected with spinal mobility may be a predisposing factor. Clinical data will be required to determine immediate factors."—*R. S. Bromer.*

Rogers, Mark H., and Cleaves, Edwin N. The adolescent sacro-iliac joint syndrome. *J. Bone & Joint Surg.*, July, 1935, *17*, 759–768.

The authors for many years have recognized a group of symptoms in patients of the adolescent age, consisting of stiffness of the low back, pain and tenderness over the sacroiliac joint, often with sciatic pain and peculiar gait due to the loss of straight leg raising. Many of them failed to improve under routine treatment and the roentgen findings were of such nature that the question was raised as to whether there was a real joint lesion, such as tuberculous or infectious arthritis. This train of symptoms tends to appear very often in stocky boys or girls who are a little overweight and who show characteristics of the Fröhlich type. The physical findings are definite. In the severe type there is a real protective list away from the side of the symptoms. On standing, the motions are restricted, forward bending is limited, while lateral bending is more restricted on one side than the other. There is localized tenderness over the posterior ligaments of the sacroiliac joint. With the patient in the recumbent position, the straight leg-raising test is very much restricted and is accompanied by pain along the sciatic nerve in some cases. On walking, there is the characteristic short-stepping gait on the side involved, which corresponds to the limitation of motion. The whole picture centers around one sacroiliac joint, tenderness, restriction of motion and sciatic pain. The latter is at times quite disabling and tends to recur on slight injuries or strain.

The roentgenograms of these patients were studied with special reference to the adolescent sacroilic joint. Small epiphyses appear along the lateral borders of the sacrum. In children, the width of the sacroiliac joints is greater than in adults. Stereoscopic exposures are helpful in showing these epiphyses. The authors studied roentgenograms of normal boys at six month intervals. They believe that the time of appearance of these epiphyses is during the fifteenth or sixteenth year. Sometimes one or both of the sacroiliac joints may have a cloudy appearance, with some irregular areas of increased density at the site of the lateral epiphyses. In these cases, the joints may be slow in assuming the adult appearance, or they may be very irregular, even suggesting pathological changes; yet, the patients have not complained of back symptoms.

Sometimes the joint may have a moth-eaten appearance; on account of the depth of the sacroiliac joints, the anterior margins may overlie the posterior margins in such a way as to confuse the picture and lead to a diagnosis of a destructive bone lesion. Usually there is change

in both joints but that which is presenting symptoms usually shows the greater change. It is also interesting to note that the symphysis pubis is sometimes slightly out of alignment, suggesting abnormal mobility in one or both sacroiliac joints. The changes resemble those noticed in Osgood-Schlatter's disease and other examples of epiphysitis or apophysitis and the authors believe that this condition which they call the "adolescent sacroiliac" is of a similar nature and should be differentiated from such lesions as tuberculosis and arthritis.

Ten cases are reported. The changes found in the roentgenograms are reproduced. The reports of the roentgen examinations came from four different offices, and they suggest that during the adolescent period there may be confusion as to diagnosis. Clinically, Rogers and Cleaves feel sure that there is a tendency to establish a wrong diagnosis and also to carry out too vigorous treatment which only perpetuates the symptoms.—*R. S. Bromer.*

MEYER, MARCEL, and GALL, MONROE B. Mycosis of the vertebral column. *J. Bone & Joint Surg.*, Oct., 1935, *17*, 857–866.

The authors review the case reports of 47 cases of actinomycosis, 12 cases of blastomycosis and one of sporotrichosis of the vertebral column. They discuss these cases, due to three different organisms, as one clinical entity. They found that the infection of the vertebrae was most often secondary to some focus in the respiratory or the digestive tracts. The vertebrae are infected either by direct contact with a suppurating focus, in which case the external surfaces of the vertebrae are eroded, or by vascular metastasis, where the bone destruction is found to be central and surrounded by a condensed ring of bone. The first possibility seems to be the case in actinomycosis; the second, in blastomycosis.

The differential diagnosis of mycosis of the vertebrae and Pott's disease, for which the former is usually mistaken, is to be made chiefly on the following grounds: (*a*) The angular deformity is most often absent in mycosis. (*b*) Mycosis shows multiple sinuses, more destructive invasion, and a more rapid opening of abscesses than in Pott's disease; the skin lesions in mycosis are characteristic. (*c*) Roentgen examination shows erosion of the cortical portion of the vertebra, erosion which is present on the articular processes and pedicles as well as on the vertebral body, or cavity formation in the cancellous portion, surrounded by a zone of increased density. None of these signs are ordinarily seen in tuberculous spondylitis. The bony rarefaction of the latter disease sometimes gives place to a dense appearance in mycosis.

The difficulty in making an early clinical diagnosis is one of the factors in the high mortality rate of mycosis of the vertebral column. The mortality rate for the collected cases was 90 per cent. However, 9 of the cases only were diagnosed during life, the remaining 51 were autopsy findings.—*R. S. Bromer.*

SHONARYEVITCH, N.B. Osteodystrophia fibrosa cystica localisata. *J. Bone & Joint Surg.*, Oct., 1935, *17*, 996–1000.

The author reports a case of localized bone cyst, occurring in a boy four years of age, located in the subtrochanteric region of the right femur. The patient was observed for a period of three years. After the first operation the cyst recurred with increased growth and greater expansion of the cortex. At the second operation the cavity in the bone was opened and a bloody brown fluid was evacuated. The edges of the cavity were covered with cyanotic granulations. A portion of the lateral wall was removed for histological examination and the cavity was thoroughly curetted. The diagnosis, histologically, was localized osteitis fibrosa cystica. Three months after the second operation the roentgenogram showed slight thickening of the upper end of the femur, the bone structure showed a more healthy character, and an increase in the strength of the bone was inferred. There was an area of transparency in the upper epiphysis of the femur but the outline of the epiphyseal cartilage of the head was beginning to appear more distinctly. The author does not discuss the etiology of the condition.—*R. S. Bromer.*

COTTINI, GIANBATTISTA. Alcuni non comuni esiti di artriti gonococciche. (Some unusual sequelae of gonorrheal arthritis.) *Arch. di radiol.*, 1935, *11*, 165–184.

The author describes 3 cases of gonorrheal arthritis, 2 of which were complicated by early calcification of the joints and the other by a myositis ossificans. Roentgenograms of the cases are given. The calcification came on in a remarkably short time after the beginning of

the arthritis, in fifteen days in one case, twenty-five days in one and twenty days in one.

He discusses the reason for the calcification in these cases without reaching any very definite conclusions. Two of the patients—the 2 who showed calcification of the joints—both had tuberculosis as well as gonorrhea. It is possible that the tuberculosis was a factor in the causation of the calcification. In the third case in which myositis ossificans occurred there had been attempts at forced flexion of the leg on the thigh; the author thinks this may have had something to do with the complication as the muscle fibers affected were the ones that had been subjected to the greatest extension. Casazza, in a description of a similar case, says that the gonococci may have a toxic-infectious action that contributes to the calcification, but there must necessarily be other factors involved as these cases are so rare.

In all the cases, in addition to the local treatment of the joints and the primary foci of infection, the author gave intravenous injections of trypaflavin. The results were good so far as the acute symptoms were concerned but the medication had no effect on the resolution of the calcification.—*Audrey G. Morgan.*

Della Santa, Antonio. Sulla visibilità diretta dei menischi del ginocchio. (The direct visibility of the menisci of the knee.) *Radiol. med.*, Oct., 1935, *22*, 929–933.

In most of the cases reported in the literature in which they were visible in the roentgenogram the menisci have been calcified. The author has examined the roentgenograms of the knee joint at the Roentgen Institute of the University of Sienna and found that in a large number of the cases in which other lesions did not hide the joint interline in the anteroposterior projection two delicate but well-defined triangular shadows could be seen at the anatomical site of both the medial and lateral menisci. The medial one was broader and lower, the lateral one narrower and higher. These roentgenograms belonged to both sexes and all ages except very young children. The roentgenograms were taken from a few days to a long time after the beginning of joint disturbances which almost always followed trauma. Illustrative roentgenograms are given.

The question arises as to why it has always been considered impossible to see the menisci in direct roentgenograms of the knee. Possibly because a delicate enough technique has not been used and also because sufficient care has not been devoted to looking for them. The author believes that the menisci are visible in the majority of cases even without calcification if sufficiently careful technique is used and they are looked for. Direct visiblity of the menisci is not only of scientific interest but it may have practical value in diagnosing pathological conditions without the use of opaque media.—*Audrey G. Morgan.*

Bristow, W. Rowley. Internal derangement of the knee joint. *J. Bone & Joint Surg.*, July, 1935, *17*, 605–626.

Bristow states that his purpose in this paper is as follows: (1) to consider certain anatomical points in connection with the knee joint; (2) to discuss the mechanism of injury to the semilunar cartilages based upon the operative findings in a large series of cases; (3) to consider certain points in the differential diagnosis of injuries to the knee joint, especially rotation sprains; (4) to describe the technique of operation, the after treatment, the complications, and the results.

The anatomy and physiology of the knee joint is very thoroughly discussed. Some of the points stressed are the fact that the knee is a complicated joint which is ill-adapted to stand rotation strains; that strain of the ligaments follows after the breakdown of the muscles, the first line of defence; that quadriceps insufficiency is not infrequently the cause of recurrent sprain of the knee joint; that the rôle of the internal lateral ligament has been unduly stressed in injuries of the cartilages; that the coronary ligaments which attach the periphery of the semilunar cartilages to the tuberosities of the tibia are thin, weak structures; that the semilunar cartilages are avascular except at the periphery and for this reason when there is a split in the substance of the cartilage, repair cannot be expected; that they are not covered with synovial membrane as it used to be thought; that the semilunar cartilages have a twofold function, thus they tend by their shape to adapt the tibial tuberosity to fit the femoral condyle and compensate for the alterations in shape of the articular surfaces between flexion and extension, and more important, they lubricate the joint surfaces.

There is no general agreement on the mechanism of cartilage injury. Three types of injury

to the knee exist which are distinct as regards mechanism and which are seldom combined:

1. Lateral strain: commonly caused by abduction of the knee, resulting in a simple strain of the internal lateral ligament or rupture of the femoral attachment of that ligament; more rarely caused by adduction of the knee, resulting in a strain or tearing of the external lateral ligament.

2. Rotation strain, which may result in a splitting of the cartilage if weight is being borne on the limb, or in damage to the coronary or other attachment, if there is no direct transmission of weight through the joint.

3. Hyperextension strain, resulting in a tear of the anterior crucial ligament or an avulsion fracture of the tibial spine.

The primary injury to the cartilage is a longitudinal tear or split in the substance of the cartilage, caused by the direct compression or grinding action of the femur on the tibia, with an added trauma caused by a rotation force, when the weight is borne on the leg with the knee flexed. The relative frequency of injury to the internal semilunar cartilage over the external semilunar cartilage is nearly five to one. Tears are of three types: complete longitudinal tear of the cartilage; posterior tear; anterior tear.

In the third part of the paper under differential diagnosis, the following conditions are discussed: recurrent displacement, loose bodies, osteochondritis dissecans, primary injury in contradistinction to recurrent injury, severe sprain of the knee joint of which extension and rotation sprains are the chief types, and injury to the retropatellar fat pad. This latter may simulate cartilage injury but is usually much less severe. There may be history of pseudo-locking, in that full extension of the knee is not permitted, but there will be no history of unlocking, characteristic of the reduction of a displaced semilunar cartilage or loose body. Local tenderness on pressure is often experienced on the joint line. The patient complains of his knee giving way. This trouble with the fat pad is more common in patients over thirty years of age. In addition to the above, Bristow discusses the differential diagnosis of overuse arthritis, torn crucial ligaments, fracture of the patella without separation, and avulsion fracture of the tibial spine.

He describes the technique of his operation devoting considerable space to the discussion of the state of the cartilages on looking into the joint. His results also are given, emphasizing the fact that results are good if the operation has been meticulously performed and the after treatment has been adequate—always provided that it was a torn cartilage which was the cause of the patient's disability.—*R. S. Bromer.*

CAMPBELL, WILLIS C. Osteogenic sarcoma. *J. Bone & Joint Surg.*, Oct., 1935, *17*, 827–843.

Campbell states that, strictly speaking, there is only one primary malignant bone tumor, osteogenic sarcoma; for other tumors arising in bone, such as myelomata, are derived from tissues residing in bone (marrow, blood vessels, etc.) that are not capable of producing bone or any tissue found in the evolutionary process of bone production. Osteogenic sarcoma is of more frequent occurrence than any tumor in bone. There is much doubt as to the origin of bone tumors, Ewing's tumor included. Jaffe and others believe Ewing's tumor to be of osteogenic origin which, if proved, would materially increase the percentage of osteogenic sarcoma. A giant cell tumor, in which malignant variants occur, is now thought to be osteogenic in origin, that is an osteoclastoma.

Osteogenic sarcoma is comprised of a combination of two or more of the elements found in the evolutionary process of bone production. In the past, the predominating elements have been employed to designate the pathological entity, but, as there may be different elements in different portions of the tumor, and many combinations of various types of cells and tissues, much unnecessary confusion has existed. The diagnosis should first be made of osteogenic sarcoma, after which any qualifying term may be employed to define the individual characteristics.

Campbell's classification is as follows:

1. Evolutionary (chondromyxosarcoma and other varieties) primary and secondary.
2. Osteoblastic
3. Osteolytic.
4. Osteolytic (medullary) in patients under twenty-five years of age.

The term evolutionary is applied to two groups, primary and secondary, as the clinical symptoms and signs are quite similar but the pathology, as revealed by the microscope, varies.

1. Primary evolutionary sarcoma, when composed of cartilaginous and myxomatous tissue (chondromyxosarcoma), may be invisible in the roentgenogram in the early stages, and the shaft of the bone may apparently be normal. The tumor, however, can be palpated and surrounds the bone. In most instances, the roentgenogram will demonstrate a definite shadow of the tumor in the soft parts and, in many cases, areas of ossification may be observed scattered irregularly throughout the mass or in spicules at right angles to the shaft. When such areas of ossification become excessive, the tumor may be designated as osteoblastic osteogenic sarcoma, the differentiation being of degree rather than of kind. In the case of the tumor described as chondroblastic, the roentgenogram may also demonstrate no abnormality in the early stage, but later there appear opaque areas of mottling, disintegration of the shaft, and invasion of the epiphysis. Sun-ray formation of bone with spicules of bone at right angles to the shaft may also be present. The so-called lipping or outgrowth of the periosteum at the junction of the shaft and the tumor is frequently observed in all types of osteogenic sarcomata, but is by no means pathognomonic as some observers suggest. Lipping, however, is most suggestive of malignancy.

2. Secondary evolutionary osteogenic sarcoma. These sarcomata arise at sites of lesions, usually benign, such as, low grade osteitis, Paget's disease, chondroma and osteochondroma. Campbell believes that these benign tumors do not undergo malignant degeneration, but the malignant process arises from dormant embryonic rests within the original lesions. As in the primary type, the histopathology is not uniform; more often it is that of a chondromyosarcoma.

3. Osteogenic osteolytic sarcoma. From a clinical aspect, Campbell divides this group into two sections: (1) children and young adults; (2) mature adults, over the age of twenty-five.

In the case of children and young adults, osteolytic sarcoma is more often found between the ages of ten and twenty years. Fever and leukocytosis are not uncommon, and at times enlargement of the lymph glands occurs. Pain is present before the cortex disintegrates; after this the pain is of low grade. In other types of sarcoma which increase in size within the unyielding shaft and periosteum, intraosseous pressure is excessive with characteristic intense boring pain. The definite mass surrounding the bone is not tender, as a rule, to pressure. The occurrence is by far more frequent in the upper third of the humerus. In the early stages, the roentgenogram may show central disintegration only, with a cavity which may resemble a cyst, but usually, when the patient is first observed, there is complete disintegration of the shaft without osseous reaction on the part of the bone or periosteum. After a pathological fracture, however, there may be some evidence of callus. The appearance is so characteristic that the diagnosis can usually be made by the roentgenogram alone. The mortality of this group is very high.

In mature adults, Campbell thinks osteolytic osteogenic sarcoma is an entirely different tumor and conforms to the old description of medullary or endosteal sarcoma by Bloodgood and others. They are not so malignant as those found in the young, and like evolutionary osteogenic sarcoma, the pathology is not uniform. The onset and evolution are slow and insidious. It has been suggested that it is secondary to some other process. The location in the metaphysis is the same as in the osteolytic type in the young, but the tumor remains largely confined within the shaft for a much longer period of time. A penetration of the shaft with irregular tumefaction externally does occur, but there is never the extensive tumefaction surrounding the disintegrated shaft which is seen in the osteolytic type in the young. This type has been mistaken for giant cell tumor, but there is not, as a rule, the multilocular cystic appearance observed in giant cell tumor.

Campbell gives his end-results and feels that they are much better than those obtained one or two decades ago, when there were no living patients to consider except mature adults. From his analysis, the chances are that any malignant tumor of bone in a child is osteogenic, osteogenic osteolytic, or a Ewing's tumor.—*R. S. Bromer.*

ROENTGEN AND RADIUM THERAPY

Montesi, Amerigo. La roentgenterapia nella leismaniosi cutanea. (Roentgen treatment of skin leishmaniosis.) *Arch. di radiol.*, 1935, *11*, 185–205.

The author describes 5 cases of leishmaniosis which he treated successfully with roentgen ir-

radiation. Photographs of the patients are given. They were from five to thirty-nine years of age. The lesions consisted of infiltrated areas, nodules or ulcerated nodules in the fluid from which *Leishmania tropica* could be demonstrated. He gave ½ to ⅔ of a skin erythema dose with a tension of 150 kv., filter 4 mm. aluminum, focus-skin distance 23 cm. The irradiation was repeated three or four times with intervals of about three weeks between irradiations. The lesions were cured without leaving scars. The lesions were old and had been growing worse. In one case they had persisted for two years.—*Audrey G. Morgan.*

MEMBERS OF THE LIVERPOOL MEDICAL RESEARCH ORGANIZATION, DIRECTOR, M. DATNOW. An investigation of the value of lead compounds in the treatment of malignant tumours. *Am. J. Cancer*, July, 1935, *24*, 531–548.

The details of the preparation of 27 organo-lead compounds are described. Each preparation was used in the experimental treatment of a group of rabbits on which the Brown-Pearce rabbit tumor had been satisfactorily engrafted. The carcinotropic action of the various compounds together with their toxic manifestations were carefully noted and comparisons made with adequate controls.

While endeavoring to lower the toxicity of these preparations, the authors' attention was drawn to the value of sodium thiosulphate for reducing the poisonous effects of heavy metals. Its value is enhanced by the property of this salt to form with lead salts complexions which increase considerably the solubility of the lead salt.

It was found, also, that the substitution of the amino-group was frequently beneficial, the most efficacious substitute being the aryl-sulphonyl radicle. A number of partially tested and unsatisfactory compounds are described in detail.

After the completion of their experimental investigations of the various compounds, the ones possessing carcinotropic action with minimal toxicity were employed in the treatment of patients with malignant disease. The results, which are not reported in this paper, are thus far encouraging to the investigators.—*E. E. Downs.*

SINGLETON, ALBERT O. Cancer of the face and oral cavity: surgery versus radiation. *South. M. J.* July, 1935, *28*, 615–619.

A comparative study was made of patients with carcinoma of the face, lip, tongue and oral cavity as treated in the periods 1912–1920 and 1922–1930. An increasing mortality found is explained by the stage of the disease in which the patients were received and not as due to therapeutic variations. The benefits offered by surgery and by irradiation are discussed. In the general hospital every cancer patient should have the benefit of the combined efforts of the departments of surgery, radiology and pathology.—*W. R. Brooksher.*

BRUNSCHWIG, ALEXANDER. Observations on the administration of large doses of calcium in metastatic carcinoma in bone. *Am. J. Cancer*, Dec., 1935, *25*, 721–729.

Many investigators have reported that calcium has an inhibiting influence on tumor growth and that calcium salts, when administered to animals by various routes, delay the appearance of transplanted tumors and slow down their subsequent growth. Treatment of tumor tissue with calcium salts in vitro prior to inoculation into animals inhibits tumor growth. Culture of neoplastic tissue in vitro is inhibited by calcium salts in concentrations that do not inhibit growth of normal tissue. Behan has reported that calcium therapy is of distinct value in alleviating pain accompanying advanced cancer.

Calcium in relatively large doses was administered to a number of patients exhibiting advanced malignant neoplastic disease of various organs. Two of these cases having bone metastasis secondary to carcinoma of the breast are reported in detail. It was noted that there was a partial or almost complete filling in of many of the osteolytic lesions by bone, also that the severe pain accompanying these lesions was greatly relieved for long periods. No opiates nor other analgesics were administered during the periods of symptomatic improvement. In one case there was a return to normal physical activity for one and a half years. No roentgen therapy was administered to these patients during or prior to the periods in which temporary sclerosis of the skeleton occurred.—*E. E. Downs.*

Geschickter, Charles F. Treatment of giant-cell tumors of the long bones. A. By surgery; B. By irradiation. *J. Bone & Joint Surg.*, July, 1935, *17*, 550–551.

Before 1910 in the United States the majority of giant cell tumors were interpreted as sarcomata and treated as such. Due to the efforts of Bloodgood and others their recognition as benign tumors became more widespread and conservative surgery, most often curettage, was advocated. In the last decade, treatment has passed from radical surgery to the other extreme of no surgery at all. At present, the prevailing types of treatments are curettage and irradiation. From a purely personal standpoint, surgeons are apt to prefer surgery, and radiologists, irradiation. It is Geschickter's belief that a point has been reached where a middle ground can be taken between the two schools.

He thinks that there are three groups of giant cell tumors in which irradiation is preferable. The bone cyst on the shaft side of the epiphyseal line, with a short duration of symptoms, in young individuals may contain a great deal of giant cell tissue, this being the so-called giant cell variant of the bone cyst. Irradiation is usually successful in accelerating healing and, where properly given, does not interfere with the growth of the epiphysis. In the second group of tumors, the patients usually elderly adults, the tumor is relatively late and there is pronounced destruction of bone. If a weight-bearing bone is involved, the probability of restoring function by surgery is doubtful, and if irradiation is unsuccessful, surgery still remains to be tried. In the third group are the giant cell tumors of the spine, especially cervical and lumbar areas and those located in the temporal area of the skull. At such sites recurrences after surgery occur in one-third of the cases.

He emphasizes four important factors to be considered by the practitioner before proceeding with treatment of suspected giant cell tumor: (1) the question of the possibility of making a correct diagnosis without the aid of biopsy; (2) the determination before proceeding with surgery of the amount of available healthy, active bone; (3) the importance of the involved bone with respect to the function of the limb; (4) the possibility of performing a thorough surgical removal of the lesion, without impairment of function. The latter should outweigh all other considerations.

In a follow-up of 300 cases treated by various methods, the percentage of successful results was highest where resection had been performed.—*R. S. Bromer.*

Cola G., and Grado, G. Ulteriori contributi alla roentgenterapia della tubercolosi polmonare. (Roentgen therapy of pulmonary tuberculosis.) *Arch. di radiol.*, 1935, *11*, 249-279.

The authors discuss their results in the treatment of 94 cases of tuberculosis by roentgen irradiation. Eighteen of them were treated by irradiation of the spleen, 12 by irradiation of the lungs and 64 by irradiation of both lungs and spleen. In most of the cases the other ordinary treatments of tuberculosis were used also—rest, diet, fresh air and tonic treatment. Twenty-two of the patients were treated in the hospital, 72 as out-patients. Careful watch was kept of weight, general condition, appetite, night sweats, thoracic pain, etc. The technique of irradiation of the spleen was spark gap, 35 cm., 1.5 ma., focus-skin distance 15 cm., filter 3 mm. aluminum, lateral field, dose 1 H, treatments once a week. In the first few cases twelve treatments were given, after that five, as it was found that with more than five or six treatments there are no further changes in the blood. The lungs were irradiated as follows: spark gap 35 cm., 1.5 ma., focus-skin distance 35 cm. posteriorly and 30 cm. anteriorly, filter 0.5 mm. copper and 1 mm. aluminum. A single posterior field was used and three anterior ones, one supraclavicular, one subclavicular and one at the base. The dose varied from 10 to 30 per cent of a skin erythema dose, depending on the case; twelve weekly treatments were given and then after an interval of two to three months the series was repeated.

The best results were obtained with the mixed treatment of both spleen and lungs and in proliferative, fibrous and adenopathic forms of tuberculosis. The authors conclude that next to pneumothorax roentgen therapy is the most effective treatment of pulmonary tuberculosis. —*Audrey G. Morgan.*

Montefusco, Corrado. La roentgen-irradiazione temporale nel diabete mellito; influenza sul ricambio idrico, idrocarbonato e clorico. (Roentgen irradiation of the temples in diabetes mellitus; its effect on water, car-

bohydrate and chloride metabolism.) *Arch. di radiol.*, 1935, *11*, 397–403.

The author describes 3 cases of diabetes mellitus in which he irradiated the temporal regions, using a total dose of 1,800 r in each case. In one case it was given in three doses of 600 r each, in one in five and in one in six doses, beginning with 200 r and ending with 600 r. The diabetes was of moderate severity. The effect on water metabolism was not uniform. There were no significant changes in glycosuria or in fasting glycemia. The elimination of chlorides in the urine was affected differently in the different cases while there were no changes of any significance in fasting chloremia. The immediate effect of the irradiation was a decrease in glycemia and an increase in chloremia.

The author concludes that the doses used by him do not have any lasting effect on the metabolism of either water, carbohydrates or chlorides, though there is a transitory action on chloremia and glycemia. It is possible that larger doses might have more pronounced effects but he does not consider the use of larger doses safe.

Tables are given showing the details of the results.—*Audrey G. Morgan.*

PALTRINIERI, GIOVANNI. Il comportamento dei setti di fronte al trattamento radiante in casi di cancro uterino. (The effect of radiotherapy of cancer of the uterus on the septa.) *Radiol. med.*, Nov., 1935, *22*, 993–1010.

The question of the resistance to irradiation of the septa between the vagina and rectum and the vagina and bladder has not been very thoroughly studied and little is known about the production of fistulas through these septa. Most authors think that such fistulas are caused by burns by the rays. The author says, however, that they are often inevitable. They are merely the results of roentgen biology and that fact should be faced and the possibility of fistulas be taken into consideration in deciding on radiotherapy for cancer of the uterus. He thinks, however, that the treatment is highly justifiable, even taking into consideration the possibility of producing fistulas.

When the first cycle of treatments is given, the difference in radiosensitiveness between the normal tissue and the cancer tissue is very great and there is little danger of causing fistulas if the tissue of the septa is not infiltrated by the malignant growth. However, in later cycles of treatment the difference in the radiosensitiveness of the normal and malignant cells decreases rapidly and may even become inverted—that is, the normal cells may become so sensitized that they are even more sensitive to the action of the rays than the cancer cells. In that case fistulas are almost certain to be produced and that is why they occur much more frequently in the later cycles than in the first cycle of treatment. This reversal of the roentgen susceptibility of the normal and cancerous cells may be due to allergic phenomena or to changes in the connective tissue or to inflammation.

There is danger in vesicovaginal fistulas of the mouths of one or both ureters becoming strangulated because of neo-plastic infiltration of the region of the trigone.

The condition of the septa should therefore be determined before giving irradiation for cancer of the uterus. If the septa are infiltrated with cancer cells, the irradiation should not be very intense so that the cancer cells may be destroyed slowly, allowing time for them to be replaced by normal tissue.

In cases of large fistulas between the rectum and vagina, it may be necessary to establish an artificial anus to save the patient the mental suffering of having the feces discharged through the vagina.—*Audrey G. Morgan.*

BONNANNO, A. M. Modificazioni ematologiche in donne con cancro dell'utero dopo applicazione di brodo vaccino e di radiazioni radium-roentgen. (Hematological modification in women with cancer of the uterus by the use of a broth vaccine and roentgen and radium irradiation.) *Arch. di. radiol.*, 1935, *11*, 325–344.

Cases are described in which women with cancer of the uterus were given a broth vaccine made of strains of bacteria taken from the flora of the cancerous uterus. Women with carcinoma of the cervix generally show an increased number of leukocytes, chiefly polymorphonuclear neutrophils and eosinophils, caused by the ulceration and suppuration of the tumor. The leukocytosis in such cases was decreased by the giving of the broth vaccine.

The local application of radium at short intervals in doses of 20 to 30 millicuries-destroyed not only caused a decrease in the size of the tumor but brought about a rapid improvement in the red blood picture, while the reaction of the white cells varied in different cases. In cases in which broth vaccine was given be-

fore the application of radium there was a marked decrease in the white cells, particularly the polymorphonuclears.

Combined treatment with roentgen and radium irradiation caused a constant decrease in the white cells and to a lesser degree in the red cells and hemoglobin. It cannot be said that the blood picture can be taken as evidence in prognosis. Generally in cases in which there was cure or temporary suspension of the disease, the blood picture showed a slight temporary anemia of the hypochromic type, sometimes accompanied by a relative increase of lymphocytes. In some cases there is no lymphocytosis and some authors hold that this is a favorable prognostic sign. The degree of anemia depends on the size of the tumor and the amount of hemorrhage caused by it.—*Audrey G. Morgan.*

Belfari-Melazzi, Teofilo. La röntgenterapia dei seminomi del testicolo. (Roentgen therapy of seminoma of the testicles.) *Radiol. med.*, Dec., 1935, *22*, 1077–1092.

The author describes 7 cases of tumor of the testicles which he has treated. He concludes that in cases of tumor of the testicle the Aschheim-Zondek reaction should be tried to demonstrate the presence of prolan A in the urine. If it is found positive it confirms the diagnosis of neoplasm. If there is only the primary tumor in the beginning stage and if it is limited to the testicle and has not invaded the tunica vaginalis, the cord or the epididymis, if the test for prolan A is positive the testicle should be removed surgically, together with the cord and the inguinal and iliac glands. Histological examination of the excised tumor should always be made and if possible abdominal prophylactic treatment given. If the tumor has infiltrated the surrounding tissues or if there are metastases, operation should not be performed but the testicle should be irradiated, taking care to protect the normal testicle. The abdominal field should be irradiated and the metastases, if there are any. If the tumor proves radioresistant, operation should be performed promptly. The patient should be kept under observation for at least three years, being examined every two or three months. If metastases develop or prolan A appears in the urine the treatment should be repeated.

Seminoma is the most frequent tumor of the testicle, constituting about 70 per cent of tumors of the testicle. They are made up of cells which morphologically resemble those of the seminal cells and are therefore radiosensitive.

The author irradiates all the lymphatic fields of the abdomen and fractionates the treatment over a period of twenty to twenty-five days. The abdomen is divided into four anterior fields by two lines, one from the xiphoid process through the umbilicus to the pubis and the other perpendicular to it through the umbilicus, and four corresponding posterior fields. There is another field over the diseased half of the scrotum. Two hundred r is given over each field per treatment, with a voltage of 180,000, intensity 2 ma., filter 0.5 mm. zinc and 3 mm. aluminum; focal distance 50 cm., until a dose of 800–1,000 r has been given on each field; two fields are irradiated a day.—*Audrey G. Morgan.*

Wolke, Knut. Über teleangiektatische Granulome und ihre Behandlung. (Telangiectatic granulomata and their treatment.) *Acta radiol.*, 1936, *17*, 117–139.

The author discusses 138 cases seen at the Radiumhemmet, Stockholm, from 1921 to 1934. In 100 cases the correct clinical diagnosis was made during life. Among the other 38 cases 10 were diagnosed as angiosarcoma, 10 as hemangiomata, 10 as benign tumors, 2 as polyps, 2 as papillomata, and 2 as carcinomata.

The histological picture in general agreed with that given in the literature. The granulomata consisted of precapillaries and capillaries, fine collagenous fibers and oval, round or spindle-shaped cells, some of them with processes. The connective tissue was arranged in coarse bundles, which divided the tumor into sections, giving it a lobulated appearance. It is generally believed that if these tumors are rich in cells they grow rapidly but this was not borne out by the experience at the Radiumhemmet. Among the 138 cases 28 were very rich in cells. Sixteen of these grew rapidly, developing in a month or less, while 7 of them developed slowly during a period of six or seven months.

These tumors are found chiefly in women and a large percentage of them develop during pregnancy, the menopause and puberty. In 19 of the cases they developed on previously existing angiomata. There was a history of trauma in 24 per cent of these cases. Hoffman and Petri

report trauma in 75 and 50 per cent respectively of their cases. Infection is probably also a predisposing factor.

Some authors hold that these tumors are true tumors, others that they are products of inflammation; the author believes they occupy an intermediate position between these two forms. There is no sharp boundary line between inflammatory changes and true tumors.

Among the cases that were treated over a year ago, 5 were treated by ordinary excision with the knife, 58 by endothermy alone, 31 by radium treatment alone and 9 by operation followed by radium treatment. Intubation was used for most of the cases of radium treatment. Two of the treated patients died within a year of treatment; the others have all survived and there has been only one recurrence. This was in one of the cases treated with endothermy and occurred six weeks after the treatment.—*Audrey G. Morgan.*

GOODFELLOW, DAVID R. Radium and the human leukocytes. *Acta radiol.*, 1936, *17*, 1–50.

Systematic studies of the blood were made in 61 cases of malignant disease in which radium treatment was given. All the cases that were given doses of any size, for example, above 4,000 milligram-hours, showed typical changes in the leukocytes which varied with the different types of treatment. Tables and graphs are given showing details of the findings.

Implantation treatment caused a marked neutrophilia followed by a progressive and severe leukopenia which affected all classes of leukocytes, except the monocytes in certain cases. Surface therapy caused equally marked changes though they developed more slowly than with the implantation method. The lymphocytes were found to be the cells most affected by irradiation and a method has been evolved by which a mathematical relationship may be established between the dosage used in a given case and the decrease in these cells in the blood.

During intensive radium treatment structural changes were generally seen in all types of leukocytes. Immature and in many cases embryonic cells appeared during periods of profound leukopenia.

The leukopenia and lymphopenia caused by therapeutic irradiation would seem to be the result of one or more of four changes, namely: (1) destruction of cells in the blood; (2) damage to lymphogenic tissue and leukopoietic organs by liberated leukotoxins, or in extreme cases by radioactive bone deposits; (3) abnormally rapid development of circulating leukocytes leading to early senility and death; (4) destruction of many lymphocytes in the circulating blood, and withdrawal of great quantities of these cells from the circulation to the bone marrow where they may develop into granulocytes in order to replenish the depleted number of these cells in the circulation.—*Audrey G. Morgan.*

CARDILLO, FURIO. Primi risultati della irradiazione rontgen a breve distanza focale—plesioröntgenterapia. (First results of roentgen irradiation with a short focal distance—plesioroentgen therapy.) *Radiol. med.*, May, 1936, *23*, 336–361.

About four years ago a new method of roentgen therapy was introduced which Perussia proposes to call plesioroentgen therapy—close roentgen therapy. Chaoul in 1931 devised a special tube for this method of roentgen treatment. He uses a focal distance of 5 cm., 50 to 60 kv. and 5 ma. The tube is described and illustrated and the technique given. This limits the volume of tissue irradiated by using soft rays, a short focal distance and a small field. It gives a dose biologically equivalent to that of radium therapy.

Among 23 cases treated in this manner the author had successful results in 22, or 95.7 per cent. These were cancers of the lip, cheek, nose and inner angle of the eye. They were all rather superficial except the one case in which the results were only palliative; in this case the cancer had involved the bone. As the treatment was begun in 1935, the late results are not as yet known. Tables are given showing the details of the author's results as well as those of Chaoul. Chaoul had 96.2 per cent recoveries in skin carcinomas and melanomas, 90.5 per cent recoveries in cancers of the lip, 50 per cent in carcinomata of the mouth and 59.1 per cent in carcinomata of the glandular organs and rectum. Total cures 59.1 per cent.

This method, like radium therapy, gives the best results in cancers of the skin and lip. There are two phases in the process of recovery—one of dry epidermitis and one of bullous epidermitis. The final healing leaves no scar. It is often hard to detect the site of the tumor. In the majority of cases a total dose of 6,000 r was

given; in a few cases only 5,000 to 5,500 r, because of intense reaction and in only one case 6,900 r. Daily treatments of 200, 300 or 400 r were given, the total dosage being given in one series.

He discusses the differences between this new method and radium therapy. While it is true that they are not the same, the new method gives at least as good results as radium therapy in the class of cases for which it is adapted. It has the advantage of being a method that can be given with a few minutes' time each day and the patient can continue his work, while for radium treatment he has to be hospitalized. It promises to be of value also in places where sufficient radium is not available. It spares the normal tissues to a greater degree than ordinary roentgen therapy.—*Audrey G. Morgan.*

Delherm, Morel-Kahn, and Targowla. A propos de la roentgenthérapie de la sclérose en plaques. (Roentgen therapy of multiple sclerosis.) *Bull et mém. Soc. de radiol. méd. de France*, Jan., 1936, *24*, 63–69.

Since 1930 the authors have treated 20 cases of multiple sclerosis at the Pitié Hospital in Paris. Of these, 13 were followed up, the remainder having received insufficient treatment. Of the 13 cases, in 4 there was marked amelioration, in 6 the amelioration was of a milder degree and in 2 there was no result; one case started the treatment just recently.

The technique of irradiation was as follows: Medium penetrating rays, with 25 to 30 cm. spark gap, 6 to 8 mm. Al, paravertebral fields, centered from the right and left to the spinal cord, the fields extending from the fourth cervical to the sixth dorsal and from the tenth dorsal to the fourth lumbar vertebra, and the series including 600 to 800 and even 1,000 r given in fractions of 200 r per seance and per field. The first series were spaced at intervals of one to two months and the later at intervals of three to six months. They were followed by additional series every six months during the first two years, and once a year after that. The encouraging results of the authors' coincide very well with those obtained by Mihailescu who in 1931 published the results in 11 cases, 5 of which have shown very marked amelioration, 3 moderate amelioration and 3 failure. Mihailescu irradiated the entire spinal cord and even the brain by more penetrating roentgen therapy (0.5 mm. Zn and 1 mm. Al) but with considerably lighter doses, corresponding to from 600 to 800 r (Solomon) per field.

The association of roentgen therapy with other routine medical methods is of paramount importance.—*T. Leucutia.*

Georgiou, Thomas. Guérison d'un cas de radio-ulcération par la radiothérapie. (Healing of a case of roentgen ulceration by roentgen therapy.) *J. de radiol. et d'électrol.*, Feb., 1936, *20*, 94–96.

A patient who suffered from Hodgkin's disease received during the period from 1924 to 1929 a total of 9 skin unit doses over an area of the back. Later a roentgen ulcer appeared which failed to respond to any conservative treatment. As a last resort the author administered a dose of roentgen rays corresponding to 5 per cent s.u.d., filtered by 3 mm. Al. The result was surprising. Within two months there was complete healing with satisfactory cicatrization which has now persisted for a period of more than a year.—*T. Leucutia.*

Kadrnka, S., and Bardet, P. Tuberculose pulmonaire aiguë, complication de la radiothérapie du cancer pharyngo-laryngé. (Acute pulmonary tuberculosis, a complication of radiotherapy of pharyngo-laryngeal cancer.) *J. de radiol. et d'électrol.*, Jan., 1936, *20*, 24–31.

Among the immediate or late local reactions incident to radiation therapy of pharyngo-laryngeal lesions, one may include edema of the larynx, hemorrhage, perichondritis, cellulitis of the neck, ulcerous radiodermatitis, chondro-radionecrosis, etc., the degree of all depending on the intensity of the dose, and extent of the radiation applied. Thanks to improvement in technique, these reactions are becoming of gradually lesser significance. In the series treated by the authors, however, a new complication was observed in connection with the lungs. The number of cases so affected was 7, four having developed various pulmonary lesions such as pneumonia, abscess and gangrene, which may represent a simple accidental occurrence, but the remaining 3 represented a condition which must be attributed directly to the effect of the rays. These 3 cases had tuberculosis of the pulmonary apex, which was aggravated by the administration of radiation therapy. The cases are described in detail and illustrated with a series of roentgenograms. It

is stated that all had very advanced cancer of the pharyngo-laryngeal structures with inoperable cervical adenopathy. This necessitated extension of the radiation fields downward below the clavicle so as to include all of the lymph glands, a fact which made the simultaneous irradiation of the pulmonary apices inevitable. It is recommended that in case of the presence of tuberculosis the radiation fields be reduced whenever possible and the irradiating beam angulated so as to leave the active tuberculous focus outside of the irradiated area.—*T. Leucutia.*

LAPEYRE. De l'efficacité de la radiothérapie dans les névralgies du trijumeau. (The efficacity of radiotherapy in trigeminal neuralgias.) *Bull. et mém. Soc. de radiol. méd. de France*, Jan., 1936, *24*, 103–107.

The article refers only to the essential trigeminal neuralgias which fail to respond to any other method of treatment. A review of the literature shows that there is a discrepancy concerning the value of roentgen therapy in this condition. According to the author this may be attributed to three causes: (1) most of the radiotherapists made no distinction beween the small neuralgias, the facial sympathalgias, and the essential grand neuralgias of the trigeminal nerve; (2) nearly always, after the first series of treatment remained unsuccessful, no further attempts were made to prolong the irradiation, and (3) there was an extreme variation in the techniques employed.

The author's personal technique is as follows: field 6×8 cm., 30 cm. skin target distance, 120 to 150 kv., 3 ma., 150 to 250 R (Solomon), two seances per week, the series including five to six seances. One single series is sufficient in most cases but if the result is unsatisfactory treatment is repeated after three or four weeks. In some cases even a third series may appear necessary. The irradiation fields include (1) the retromaxillary region, the incidence of the beam being obliquely from behind forward and slightly from downward upward at about 45°; (2) in certain instances a second field is necessary perpendicularly on the hemiface; (3) in those cases in which the pain is chiefly frontal a third field is employed to the frontotemporal region with the ray perpendicular towards the sella turcica.

Of 12 cases, in 8 there was complete cure with one series of irradiation; in 3 a complete cure following two series of irradiations; in the last case which was very severe, only marked amelioration was obtained.

The conclusion is reached that radiation therapy constitutes the method of choice in all cases of essential neuralgias of the trigeminal nerve and it is therefore recommended that it be employed routinely.—*T. Leucutia.*

SEGRE, MARIO. Il trattamento roentgen delle radicoliti cervico-brachiali da artrite deformante della colonna cervicale. (The roengten treatment of cervicobrachial radiculitis from arthritis deformans of the cervical column.) *Radiol. med.*, April, 1936, *23*, 213–226.

Seven cases are described and illustrated with roentgenograms. The author emphasizes the fact that roentgen treatment should not be used for sensory and motor disturbances of the brachial plexus unless roentgen examination has shown signs of arthritis of the cervical vertebrae, usually the lower ones, and unless other causes for the disturbance can be excluded. In cases that are caused by arthritis deformans of the cervical column roentgen treatment brings about relatively rapid recovery even in old chronic cases. The treatment is so uniformly successful that if it fails it may be used as a therapeutic test of whether the disturbance is caused by arthritis of the cervical column.

The mechanism by which arthritis deformans of the cervical column causes injury of the brachial plexus is not known, nor is the mechanism known by which roentgen irradiation cures such disturbances. There is no change in the roentgenogram of the cervical column even in cases in which roentgen treatment of the plexus symptoms has been successful.

In the treatment of these cases the author uses rays of moderate hardness—150 kv., with filters of 0.5 mm. zinc and 2 mm. aluminum. He uses one posterior field with a limitator 8×10 cm. arranged along the long axis of the column. Ordinarily a single irradiation with a surface dose of 200–250 r is sufficient. In 2 cases he gave half this dose a second time. He never saw any disturbances due to action of the rays on the thyroid. In only 2 cases there was a temporary exacerbation of the pain after the irradiation. In some cases there was no decrease of the pain for the first twenty-four

hours but in the majority there was decrease of pain immediately after the irradiation and in twenty-four hours it had stopped completely. —*Audrey G. Morgan.*

Castaño, Carlos A. Cáncer ce seno; su tratamiento. (Cancer of the breast; its treatment.) *Bol. Inst. de med. exper. para el estud. y trat. del cáncer*, Dec., 1934, *11*, 961–967.

The treatment of cancer of the breast represents one of the most important problems both from a surgical and a pathological standpoint. It is the author's opinion that the only efficacious method of treatment is radical surgery and that other auxiliary methods may be used only when there is contraindication to surgical treatment. Among these latter he enumerates the following: No operation should be attempted in acute carcinoma of the breast in a young woman at the moment of lactation, the results being always disastrous. The administration of roentgen therapy with ovarian castration, a benign and simple operation, leads to better results. Operation is also of questionable value in the atrophic scirrhous cancer of slow evolution in women over sixty, as well as in the pustulous scirrhous cancer of Velpau, associated with cancerous lymphangitis and multiple subcutaneous invasion of the skin of the thorax. Finally, operation is contraindicated in all those cases in which there is evidence of metastases to distant parts of the body.

As concerns the operative technique, this must be carried out in a most radical manner, with removal of the entire breast as well as of the pectoral muscles, and a thorough cleaning of the axillary space.

From the point of view of diagnosis, it is the author's opinion that it is dangerous to make a diagnosis of a mammary adenoma or chronic cystic mastitis in a woman past the age of forty. Every node in the breast of such a woman, especially associated with adherence to the skin, must be considered as potentially malignant and treated as such.

After considering the value of biopsy, as well as some of the more salient publications in the medical literature, the author concludes with the statement that he is opposed to postoperative prophylactic radiation therapy in carcinoma of the breast. He only irradiates cases with enlargement of the supraclavicular glands in which a regression of the enlarged glands and even a permanent cure is sometimes observed. There is at least one case under the author's observation which was operated upon in 1919 and which two years later developed metastases to the supraclavicular glands which were treated with radium and roentgen rays, the patient having remained in good health since.—*T. Leucutia.*

Riebeling, M. Terapéutica moderna de los tumores malignos primitivos del seno. (Modern therapy of primary malignant tumors of the breast.) *Rev. men. de cir.*, Jan., 1936, *1*, 277–292.

The symptomatology of mammary cancer is quite clear in the advanced stages but in the early stages a differentiation from a benign tumor may appear exceedingly difficult. It is the author's procedure in similar instances to take accurate measurements of the principal diameters of the tumor by a caliper and to repeat this examination every week for three weeks. During the same time the glands in the axilla are closely scrutinized. If, at the end of three weeks, no increase in the size of the tumor is noted and there is no evidence of glandular enlargement in the axilla, a simple endocapsular enucleation of the tumor is performed under local anesthesia. The further procedure depends then on the pathologic report. In contradistinction to this, if there is a successive enlargement of the tumor or if there are palpable glands in the axilla, the author performs an aspiration biopsy according to the technique of Martin. If the biopsy confirms the diagnosis of malignancy, treatment is immediately instituted. It may be mentioned that sometimes roentgenography of the breasts with the soft tissue exposure, as indicated by Goyanes and Lockwood, furnishes additional criteria of differentiation. Since surgery alone, even with the technique as radical as that of Halsted with the modification of Willis, has failed to notably increase the five year results during the past thirty years, it is the author's opinion that radiation therapy must always be associated with such a procedure. The author in general makes the grouping of Steinthal the basis of classification. As it concerns the irradiation, in Group I, that is when the tumor is localized to the breast, surgery alone may produce good results, but in Group II, that is, when there is evidence of ad-

hesions, ulceration and enlargement of the axillary glands, a combination of surgery and radiation therapy will lead to the best results. In Group III, when there is supraclavicular involvement or evidence of cutaneous metastases, the results are poor whatever the method of treatment.

The prognosis is especially unfavorable in young women, where the author prefers to use a combination of external roentgen therapy with interstitial application of radium. The dosage in such instances is pushed up to the uppermost limit, especially as it concerns the irradiation of the site of the tumor since the lethal dose of carcinoma of the breast is in the neighborhood of 10 to 12 S.E.D. The irradiation both with roentgen and radium therapy is given over a longer period, as a rule extending over several weeks for the roentgen therapy and six to seven days for the interstitial radium.—*T. Leucutia.*

SALOJ, CLAUDIÓ DARWIN. Tratamiento del cáncer de la glándula mamaria. (Treatment of cancer of the mammary glands.) *An. de cir.*, Nov., 1935, *1*, 125–134.

After briefly considering the various phases of surgical and radiation therapy in cancer of the breast as applied in other institutions, the author refers to a series of 22 cases of his own in which radiation therapy constituted the method of choice, with the exception of 4 in which interstitial radium was applied. Of these latter, 2 are well and 2 have died from distant metastases. Without wishing to draw the conclusion that the implantation of radium might have been responsible for the spreading of the cancer in the 2 cases who have died, he nevertheless feels safer by continuing with the roentgen therapy alone in preference to interstitial radium. The roentgen therapy consists in application of doses of 400 r repeated daily over alternating fields until a total of 1,200 r is reached over each field. The quality of the rays is that obtained with 180 kv., 1 mm. Cu and 3 mm. Al as filter. The rate of regression of the tumor is observed and treatment repeated for a second and third series, the intervals between the series depending on the general course. If the diminution of the tumor is not very pronounced radiation therapy is discontinued, otherwise it is pushed up to the uppermost limit. In a second phase of treatment, the interstitial application of radium or surgical extirpation is applied. The radium application is carried out with 2 mg. radium needles filtered by 0.5 mm. platinum which are distributed within the tumor mass as homogeneously as possible and left in situ for a period of seven to nine days. If operation is decided upon, this is performed in a very economical way with the radio knife, without removal of the pectoral muscles. After healing of the wound, postoperative roentgen therapy is resumed but with doses which are a little less than those preliminary to surgery. Of the 22 cases treated, 10 presented operable lesions, 6 were at the borderline of operability, and 6 were entirely inoperable. In 1 case the treatment was incomplete, 4 have died, and the remainder are still under observation. The 22 cases are briefly described. A perusal of these case reports, however, reveals that none of the cases antedates 1931.—*T. Leucutia.*

JOVIN, J. Criteriile de indicaţie în radioterapia fibromulu uterin. (Criteria of indication for radiotherapy of uterine fibroids.) *Bul. Soc. de radiol. şi electrol. med. din România*, No. 9, 1934, *3*, 9–15.

On the basis of 200 cases treated personally, the author establishes the following general criteria concerning the indication and relative value of surgery and radiation therapy in uterine fibroids. A suppression of the bleeding is obtained in 95 per cent and of the tumor in 80 per cent of the cases treated by irradiation, which indicates that the majority responds favorably to this type of treatment. The remaining part, however, must be subjected to surgery. In drawing the boundary between the two groups, the following rules may be established: Surgical intervention is to be preferred as a method of choice in (1) fibroma with uncertain diagnosis; (2) fibroma complicated with a torsion of the pedicle or with a calcareous or myxomatous degeneration or with a cancer of the body of the uterus; (3) fibroma complicated with other affections of the neighboring structures, and (4) voluminous fibromas reaching above the umbilicus. The other type of fibromas, which include the bulk of the cases, may be treated by roentgen therapy. A very small group is reserved for radium therapy in preference to roentgen therapy. These represent (1) fibroma in young women where only a tem-

porary castration is desired; (2) fibroma with intensive hemorrhage, and (3) fibroma complicated by carcinoma. Finally, radiation therapy, either by roentgen rays or radium, is indicated in all those cases in which operation is not feasible as, for example, diabetes, albuminuria, cardiac affections, etc.—*T. Leucutia.*

MISCELLANEOUS

Thoraeus, R. A portable secondary standard for roentgen ray measurements. *Acta radiol.*, 1935, *16*, 735–743.

A description is given of a portable secondary standard for roentgen-ray measurements built according to the electrostatic principle and equipped with a spherical graphite ionization chamber, the outside diameter of which is 16 mm. The apparatus is illustrated. The results of rather detailed calibrations and tests for the instrument described are given and discussed. It is found that for all intensities and qualities generally met with, the readings are very closely parallel with those obtained by the standard air ionization chamber, and that the accuracy obtained when measuring the intensity in r per minute is ± 3 per cent.—*Audrey G. Morgan.*

Christensen, Helge. Einige physiologische und physikalische Betrachtungen über die Leistungsfähigkeit der Durchleuchtung. (Some physiological and physical considerations in regard to the value of roentgenoscopy.) *Acta radiol.*, 1936, *17*, 169–181.

There are a number of closely related physical, physiological and psychic components involved in the method of roentgenoscopy. This article discusses visual acuity and the capacity for distinguishing differences in density, particularly with the low illumination that is used in roentgenoscopy, which may go as low as 0.001 lux. The significance of increased scattering in contrast is considered schematically and means of reducing it are discussed; the best methods are the use of the Potter-Bucky diaphragm and the interposition of a certain distance between the objecta nd the screen. For physiological reasons the field should not be too small. The unfavorable conditions under which the eye is placed in screen examination make roentgenoscopic findings more or less unreliable. There is need for great improvement in the method.—*Audrey G. Morgan.*

Gallavresi, Luigi. Ricerche microfotometriche nel campo di alcune immagini radiografiche lineari. (Microphotometric study of some lines appearing in roentgenograms.) *Radiol. med.*, July, 1935, *22*, 641–661.

The author discusses the different theories that have been advanced to explain the cause of certain stripes in roentgenograms from hyperillumination and hypoillumination. He then reports the results of his microphotometric study of the line around the outline of the thorax bounding the lung fields, called Correra's line, and the clear borders surrounding the roentgen images of gas bubbles in the intestines.

Correra's line appears when the lung fields are freed from superposition of the ribs by Palmieri's projection. It is brought about by two causes, the first physico-geometrical in nature and the second simply an optical illusion known as the Mach effect. The physico-geometrical factors, which he discusses in detail, are active only at the base of the thorax where there are conditions relative to the form of the thorax which cause a line of hypoillumination on the negative and therefore a stripe of greater transparency. In the upper part of the thorax, at the scapular girdle and the points where the pectoralis major and the latissimus dorsi muscles reach their greatest development these physico-geometrical conditions are lacking and therefore the lines here are due to the Mach effect. Of course, this effect may reinforce the lines at the base also where the line is an optical reality. But the line may appear without any geometrical factor simply as an optical illusion. This is confirmed by the transparent rings around the roentgen images of gas bubbles in the intestines; these rings are in the great majority of cases optical illusions.—*Audrey G. Morgan.*

Licht, Eric de Fine. Screening as compared with roentgenography in examination of the lungs. *Acta radiol.*, 1936, *17*, 105–116.

The author reviews the literature on the comparative value of roentgenoscopy and roentgenography in examination of the lungs. From the literature and the results of his own experience he comes to the conclusion that screen examination is quite unreliable and should not be depended on without the taking of roentgenograms. In roentgenoscopy of the

lungs very feeble illumination is used The author believes that the frequent overlooking of even quite serious pathological changes when only roentgenoscopy is used is due to this fact. Visual capacity is greatly reduced in poor illumination. The decisive factor in this is not a reduction of the capacity for perceiving form but rather a reduced capacity for perceiving differences in density of contrast. This has been shown by examinations made by Stumpf and by the author himself.

He believes that in all cases with clinical symptoms of lung disease roentgenograms should be made. Roentgenoscopy alone should be used only in mass examinations and then only with caution.—*Audrey G. Morgan.*

TALIA, FERDINANDO. La doppia esposizione della pellicola radiografica nella pratica radiologica. (Double exposure of the roentgen film in roentgen practice.) *Arch. di radiol.*, 1935, *11*, 365–378.

Double exposure of the roentgen film is of value in studying certain conditions. The author takes the first exposure by the technique usually used for the region in question, exposing the part for one-third less than the time normally used; the second roentgenogram on the same negative is then taken in the same way with an exposure a little less than usual. Inversion of this method or taking the two roentgenograms with approximately equal exposure times gives less contrast.

Salotti used the double exposure with one in the erect and one in the prone position and with one in forced inspiration and the other in expiration. The author has tested these methods and finds them useful. He gives roentgenograms showing the position of the abdominal organs in the two exposures.

This method of double exposure gives useful information in regard to the ligaments and tonus of the viscera, the relations between the different abdominal organs, particularly when there are deviations due to the constitutional habitus of the subject; the diagnosis of the site and extent of perivisceral processes; the mobility of foreign bodies in cavities, particularly the orbit and in the study of the depth of foreign bodies.—*Audrey G. Morgan.*

BENASSI, ENRICO. Un esempio di applicazione della radiologia ad indagini giudiziarie non mediche. (An example of the use of roentgen examination in non-medical legal questions.) *Arch. di radiol.*, 1935, *11*, 345–347.

The author describes a case in which roentgen examination was used in a non-medical legal case. It was in a trial for homicide and the defense wished to prove that the death had not been a murder but a hunting accident. The questions to be settled by roentgen examination were whether branches of trees from the site of the death contained gunshot; the depth of the shot for the purpose of giving ballistic evidence as to the distance from which the shot had been fired and the course followed by the projectiles, or rather their position with relation to the point where they entered the wood in order to determine whether they came from one shot or from two fired from different places. These questions were answered satisfactorily by the roentgen examination. Roentgenograms are given of the branches containing the shot which had penetrated the wood to a depth of 6 to 7 mm.—*Audrey G. Morgan.*

VAJANO, DOMENICO. L'azione a distanza delle iniezioni endovenose di biossido di torio colloidale. (The late effects of intravenous injections of colloidal thorium dioxide.) *Arch. di radiol.*, 1935, *11*, 127–142.

The author has previously reported experiments in hepatosplenography with thorotrast. In this article he reports the results of roentgen and histological examination of rabbits and guinea pigs three years after the preparation had been given. He found on roentgen examination that the thorium shows a certain tendency to accumulate in the liver about a year and a half after its administration; it collects around the periphery of the lobules. Roentgenograms of the liver and spleen taken three years after the administration of the thorium show practically as dense a shadow as those taken soon after its administration. Histological examination showed that beginning thirteen to fourteen months after the injections the thorium has a tendency to accumulate at the periphery of the liver lobules and in Kiernan's spaces and in the follicles of the spleen. In animals inoculated with normal doses of thorotrast (1.5 to 3 c.c. per kilogram), there were no true changes in the parenchyma of the organs that fix the thorium, but only persistent hypertrophy and hyperplasia of the reticulo-histiocytic cells of

the liver and spleen and a slight degree of thickening of the connective tissue stroma of the spleen. But in animals treated with larger doses, there are more or less marked degenerative changes in the parenchyma of the liver, kidneys and spleen, but generally less intense than those found soon after the injections in animals that have been treated with the same doses.

There seems to be no doubt from the findings that the thorium is eliminated. The elimination seems to take place at first through the liver and kidney but later only through the liver. The elimination is very slow, however, and it is impossible to say from the examinations after three years whether total elimination of the thorium will ever be effected and if so in what time. As used normally for roentgen demonstration of the liver and spleen, thorotrast may be said to be practically non-toxic, but it is possible that its radioactive power may later produce anatomical changes in the organs.—*Audrey G. Morgan.*

Chiara, Giuseppe; Caponnetto, Andrea, and Nicotra, Antonio. Studio dei linfatici della capsula adiposa del rene con preparati colloidali di torio. (Study of the lymphatics of the fatty capsule of the kidney by means of colloidal thorium preparations.) *Radiol. med.*, Jan., 1936, *17*, 26–29.

The authors describe experiments on 4 dogs in which they injected 6 to 10 c.c. undiluted thorotrast or thoriofanin directly into the fatty capsule of the kidneys. Roentgenograms were made 6 hours and 5, 10, 15, 20 and 30 days after the operation.

They found that the lymphatics of the fatty capsule of the kidney do not anastomose either with the superficial lymphatics or with the deep lymphatics in the substance of the kidney. The lymphatics of the capsule on one side did not show any connection with those of the capsule on the other side. The lymphatics of the fatty capsule seem to flow for the most part into the para-aortic and subdiaphragmatic lymph glands of the same side.

The thorium is not stored in the fatty cells. It collects in the interlobular and intercellular connective tissue, particularly around the vessels. The authors did not observe any elimination of the thorium through the kidney.—*Audrey G. Morgan.*

Chiara, Giuseppe; Caponnetto, Andrea; and Nicotra, Antonino. Tentativi di visualizzazione radiografica delle vie linfatiche tra i seni frontali e le meningi. (Attempts at roentgen visualization of the lymphatic tracts between the frontal sinuses and the meninges.) *Radiol. med.*, Dec., 1935, *22*, 1092–1096.

The authors describe experiments made in an attempt to render the lymphatic tracts between the frontal sinuses and the meninges visible roentgenologically. They used dogs as the experimental animals and colloidal thorium as the contrast medium. Owing to technical difficulties, which are described, they could not demonstrate centripetal tracts from the sinuses to the meninges. The negative results in these cases were not necessarily due to the absence of such tracts but may have been due to the technical difficulties. On injecting the contrast medium into the subdural or subarachnoid spaces to demonstrate centrifugal tracts from the meninges to the sinus, they found that the sulci and convolutions of the brain were rendered visible and that thorium appeared in the lateral cervical glands but there was no opacification of the frontal sinus. They conclude therefore that there are no lymphatic tracts from the meninges to the frontal sinus.—*Audrey G. Morgan.*

Overgaard, Kristian. Experimentelles über kurz- und ultrakurzwellentherapie bösartiger Tumoren. (Experimental work on short and ultrashort wave therapy of malignant tumors.) *Acta radiol.*, 1936, *17*, 182–190.

Experiments on white mice are described which demonstrate that treatment with short and ultrashort waves had a therapeutic action on implanted tumors. The effect of this treatment is the same as that of treatment with ordinary diathermy. It is due evidently simply to the action of heat, to which tumor tissue is less resistant than are the normal tissues of the body.—*Audrey G. Morgan.*

Rocchini, Giuseppe, and Calchi-Novati, Giulio. Funzionalità renale ed onde corte. (Kidney function and short waves.) *Radiol. med.*, April, 1936, *23*, 240–254.

The authors studied the effect of short waves on kidney secretion, testing secretion with the

phenolsulphonphthalein test and the dilution test. The technique of the tests is described and tables given showing the details of the results. They found that the application of short waves to the kidneys has the following effects: (1) reduction of the amount of phenolphthalein excreted; (2) decrease of the amount of water eliminated; (3) percentage increase of the concentration of urinary urea, not sufficient however to equal the total urea output found in control tests; (4) decrease of the absolute and relative amounts of chlorides excreted.

These phenomena are seen both in normal and pathological kidneys. They are caused only by the application of short waves to the kidney region and are not therefore due to reflex phenomena or to general changes in the organism. These phenomena are probably caused by vasodilatation and venous stasis brought about directly by the action of the short waves on the kidney circulation. No specific action for waves of special lengths could be discovered, nor does the heat factor seem to be the cause of the phenomena. The response of the organ is not strictly proportional to the intensity of the electromagnetic radiation applied. The phenomena, however, seem to be a specific biological reaction of the kidney to the special type of stimulus given by the short waves.—*Audrey G. Morgan.*

CHROM, SV. A. Studies of the effect of roentgen rays upon the intestinal epithelium and upon the reticulo-endothelial cells of the liver and spleen. *Acta radiol.*, 1935, *16*, 641–660.

Mice were irradiated with a Siemens-Schuckert stabilovolt apparatus, 160 kv., 4 ma. The distance in most cases was 42 cm., making the intensity of the irradiation 12.4 r/min. All the irradiations, general as well as local, were given through a filter of 0.5 mm. copper and 3 mm. aluminum. In the general irradiation, doses of from 250 to 550 r were given and autopsy and bacteriological examination performed three to ten days later. The abdominal organs and heart's blood were found infected with bacteria that are normally found in the intestine. When local irradiation was applied only over the intestine in doses of 550 r, the lymphatics of the intestine were moderately infected with colon bacilli in about half the cases but cultures of the organs and blood showed no growth of bacteria. There was therefore a distinct difference in the effects of local and general irradiation. There was also a great difference in the mortality of the irradiated animals in the two groups. Fifty to 80 per cent of the animals given general irradiation of 550 r died spontaneously while local irradiation up to 1,100 r killed only 4 out of 24 animals.

In order to study the action of the reticulo-endothelial cells of the liver and spleen the whole abdomen, including the liver and spleen, was irradiated and about seventy-two hours later intravenous injections of Breslau bacilli given. Control animals that were not irradiated were given the same injections. General irradiation with a dose of 450 r showed a decided decrease in the capacity of the body to filter off the injected bacilli. Apparently the phagocytosis carried out by the reticulo-endothelial cells is of decided importance in combating infection.

Histological examinations were made of various parts of the intestinal tract after general and local irradiation. There was no special difference in the pictures after general and local irradiation; it seems probable, therefore, that the permeability of the intestinal epithelium to bacteria is caused by a direct action of the rays. The epithelial cells, particularly those in the ileocecal part of the intestine, after irradiation seem to become permeable to the bacteria normally found only in the intestine.

The author concludes from his experiments that the roentgen death that often occurs in experimental animals is caused by several factors, including anemia, intoxication and enterogenous bacteremia. In most cases it is impossible to say which of these factors is immediately responsible for the death.—*Audrey G. Morgan.*

SEELIG, M. G., ECKERT, CLARENCE T., and COOPER, ZOLA K. The relationship between vascularity and the reaction to radium of squamous epithelium. *Am. J. Cancer*, Nov., 1935, *25*, 585–591.

A satisfactory explanation of the mechanism of tissue changes following irradiation has not been furnished. How much of the effect of irradiation is direct and purely local upon the cells, and how much is indirect and dependent either upon induced vascular changes or upon some general response of the organism is difficult to say. The experimental study here reported was prompted by the fact that in the literature there is this striking diversity of

opinion regarding the rôle played by vascularity as an agency in the action of radium on tumors.

A number of authors are mentioned who argue that the effect of irradiation is due to direct changes in the cancer cells, while a number of others believe that the changes in the tumor are secondary to an alteration in its vascularization.

A method is described for compromising the circulation of a portion of rabbit's ears. After the viability of the flap had been established the dorsal surface was exposed to 100 mg-hr. of radiation. A 50 mg. capsule of radium was employed as a source. A similar amount was placed on the normal ear and biopsy specimens made at the end of 24, 48, 72, and 96 hours.

Summarizing the experimental work, the authors state that the effects produced by irradiation of the vascularly compromised tissue when compared with those following similar irradiation of control normal areas are not dissimilar. The vascular compromise of the skin epithelium of the ears in this series of rabbits did not alter its radiosensitivity. Radiosensitivity seems to be an inherent quality of the cell which varies even in individuals of the same species.—*E. E. Downs.*

Snellman, Björn. Attempt to develop reduced radio-sensitivity in Jensen rat sarcoma by means of roentgen irradiation. *Acta radiol.*, 1935, *16*, 545–556.

The author gives a brief review of the most important opinions in regard to the phenomenon of acquired reduced radiosensitiveness in malignant tumors, and reviews some experimental work which throws light on this question directly or indirectly.

He describes the technique of irradiation which he used and gives the lethal dose in vivo for the laboratory strain of Jensen rat sarcoma as 4,000 to 4,500 r.

He irradiated Jensen tumors in vivo with sublethal doses of roentgen rays and found reduced radiosensitiveness in most of the descendants of the tumors which had been irradiated previously. The facts indicate that this reduced radiosensitiveness is a direct result of the effect of irradiation on the tumor cells themselves. The reduced radiosensitiveness is accompanied by slower growth, lower incidence, a higher content of collagen substances and a smaller number of mitoses.—*Audrey G. Morgan*

Wilson, C. W. Some effects of the gamma rays of radium on the developing chick embryo. *Acta radiol.*, 1935, *16*, 719–734.

An arrangement of radium needles suitable for the approximately uniform irradiation of chick embryos one to six days old is described. Graphic relations are determined between the age of the embryo and its radiosensitiveness as measured by two different methods. Radiosensitiveness decreases uniformly and slowly for the first three days, more rapidly from the third to the fifth day and then remains fairly stationary. These findings may be due to the varying rate of growth of the embryos. There seems to be a maximum dose of gamma radiation from which embryos may recover and hatch and this seems to have the same value for all embryos of from one to six days' incubation. The death of the embryos in the shell is probably caused by disturbances in the blood circulation.

Roentgen and radium rays seem to have different effects on developing chick embryos. With roentgen rays, when the same dose of radiation is given to both one day and six day embryos and these are allowed to incubate for another twenty-four hours, the effects on the older embryos are very much more severe than on the younger ones. With radium rays, however, it was found that five times as large a dose was required to cause death of the six day embryo as of the one day embryo. Moreover if six day embryos are exposed to radium for five hours (the lethal exposure for one day embryos) the embryos appear macroscopically to be quite normal.—*Audrey G. Morgan.*

Epifanio, Giuseppe. Azione biologica dei "neutroni." Nota preventiva. (Preliminary note on the biological action of "neutrons.") *Radiol. med.*, May, 1936, *23*, 367–368.

These neutrons are beryllium emanations screened with 7 mm. of lead. They were placed on the lesions to be treated. Two cases of recurrent carcinoma of the breast with ulcerated nodules were treated and 2 cases of skin epithelioma, one on the forehead and one in the nasolabial fold. They healed in a time varying from one to two months. The course and type of healing were practically the same as those seen in radium treatment. The object of the 7 mm. lead screen was to exclude gamma and ultragamma radiation so that the action of the neutrons uninfluenced by other rays could be

judged. A platinum screen should be used to get the combined effect of all the rays. The author did not have a large enough amount of the material on hand so that large tumor masses could be treated but the biological effects would doubtless be the same. The interposition of a layer of paraffin between the lead and the surface to be treated did not prove to be of any special value. The neutrons have been shown to have a much greater penetrating action than gamma rays. The material is much cheaper than radium.—*Audrey G. Morgan.*

PARKER, H. M. The dependence of the back-scattering of roentgen rays in a phantom on focal distance, quality of radiation and field size. *Acta radiol.*, 1935, *16*, 705–715.

Although considerable attention has been given to the question of the percentage back-scattering of roentgen rays at the surface of a scattering medium, the more general problem of the amount of scattering at various points within the scattering body has been relatively neglected.

The author designates the total radiation as I_t and the scattered irradiation as I_s and tabulates the value of the quotient I_s/I_t for different focal distances, qualities of radiation and field sizes. Tables and curves are given showing the details. The values are given for half-value layers of from 0.32 to 3.3 mm. I_s/I_t at any distance is independent of the focal distance and decreases regularly with increasing hardness of the radiation.

A number of points of interest in deep therapy arise from the measurement of this back-scattering coefficient. In the first place, the dose at a depth in the phantom receives a far greater amount from back-scattering than might be supposed. Even with a field as small as 19.6 sq. cm. and at a normal half-value layer of 1.5 mm. copper scattering at a depth of 10 cm. constitutes 54 per cent of the total radiation. With a field of 300 sq. cm. the amount has risen to 81 per cent. It follows that in the application of the rays to the human body the presence of bone masses or air cavities may have an appreciable influence on the dose applied to the tumor as compared with that calculated from isodose charts. Hence extensive measurements of the radiation at various points of a cadaver or fairly complete models of the body might profitably be undertaken as an aid to more exact dosage.

The rapid decrease of I_s/I_t in the superficial layers between a half-value layer of 1.1 and 1.8 mm. copper offers suitable conditions for examining the possible variations of erythema with quality of radiation, a problem which does not seem to have been satisfactorily settled as yet. In progressing to the harder of these two radiations, not only is the primary hardness increased but there is a notable decrease in back-scattering which must necessarily be of a softer character. The average composition of the radiation in the first 5 mm. is therefore quite different. Furthermore with a roentgen apparatus operating at 250 kv. it is easily possible to obtain the two radiations at equal intensity and the range is so limited that errors in dosimetry are not likely to be important.

Increase of field size produces a less rapid increase of I_s/I_t for the hard radiation, in accordance with the increased forward concentration of the scattered radiation. The cut-off at the edge of the beam is therefore better defined for the hard radiation. This may prove to be a valuable asset in high voltage irradiation, especially where narrow fields have to be directed just to miss vital structures. Reduced scattering from the main beam is automatically combined with increased homogeneity in it.—*Audrey G. Morgan.*

SPIEGLER, G. Die Streustrahlung in ihrer Wirkung auf die Bildgebung. (The effect of scattered radiation on the roentgenogram.) *Fortschr. a. d. Geb. d. Röntgenstrahlen*, May, 1935, *51*, 498.

Spiegler presents some roentgenograms made with and without scattered radiation. The roentgenogram is the result of zones in which scattered radiation is effective and others in which it is absent or less effective. Loss of detail should not equal the width of the half shadow with increasing widening of the transitional zone and in distinctness decreases after reaching a maximum. The author also discusses the relationship of contrast to object-film distance. The roentgenogram is a combination of factors which produce sharp and blurred images. A scheme is presented for correlating degrees of density with the underlying physical conditions.—*E. T. Leddy.*

THORAEUS, R. The wall-thickness of roentgen tubes and its influence on the filtration in general and on the function of the tin filter in special. *Acta radiol.*, 1936, *17*, 161–167.

This article describes an experimental study of the thickness of the wall of roentgen tubes and its effect on the function of some filters, particularly the normal tin filter. This study was carried out by means of a method of artificially varying the thickness of the wall of the same tube that had been tested experimentally.

It was found that the half-value layer of the beam behind the tin filter is not influenced by changes in the thickness of the wall of the tube, but the thickness of a copper filter under the same conditions must be corrected more or less in order to get a constant half-value layer. It was also found, as was to be expected, that the superiority of the tin filter is somewhat reduced with increasing thickness of the wall and that increasing the thickness of the wall has an unfavorable effect on the intensity of the beam.

An increase by filtration in the penetrating power of a roentgen beam is always associated with a loss of intensity. The chief question in the filtration problem, therefore, is how to obtain a desired quality with the smallest possible loss of intensity. Properly constructed tin filters are no doubt the most economical ones for all voltages from 150 kv. up to at least 400 kv. and probably higher.—*Audrey G. Morgan.*

Gilardoni, Arturo. Controllo dei tempi d'esposizione radiografici con metodo elettrolitico. (Control of the time of roentgen exposure by an electrolytic method.) *Radiol. med.*, April, 1936, *23*, 262–264.

A method for the control of the exposure time of roentgen films based on the electrolytic action of an alternating current is described and illustrated. This method is better than the classical method, particularly when many films are to be taken.—*Audrey G. Morgan.*

Boström, G. The effect of 1:2:5:6 dibenzanthracene on tissue metabolism in mice previously treated with this substance. *Acta radiol.*, 1935, *16*, 224–232.

The author treated mice with 1:2:5:6 dibenzanthracene and then treated slices of live substance in vitro with this substance, estimating the effect on liver metabolism by the Warburg method. The effect on oxidation was tested in 6 mice, 3 of which showed first a rise and then a fall of oxidation after the addition of 0.1 c.c. or 0.02 and 0.002 per cent dibenzanthracene suspension. In the other 3 cases and in 5 untreated controls the suspension had no effect on oxidation.

The effect on anaerobic glycolysis was tested in 6 cases, in all of which 0.1 c.c. of an 0.02 per cent dibenzanthracene suspension produced a marked inhibition; 1/10 of this dose produced a slighter fall and 1/100 gave no reaction in 5 cases and an increase of lactic acid formation in one case.

The experiments were made with the object of determining the type of tissue metabolism in animals treated with carcinogenic compounds and also of determining whether, after a period of administration of such hydrocarbons, there was a change in the reaction to the substance in question. According to a hypothesis proposed by O. Reuterwall the carcinogenic factor should produce an allergic form of change in the tissues, and the chronic irritation which is believed by many to be the cause of cancer, would be due to anaphylactic and allergic or related phenomena. The experiments so far do not show that it is possible to produce allergy in mice with 1:2:5:6 dibenzanthracene.—*Audrey G. Morgan.*

Santesson, Lars. Projet de méthode permettant de mesurer exactement l'activité protéolytique des tissus cultivés in vitro. (Proposed method of measuring accurately the proteolytic activity of tissues cultivated in vitro.) *Acta radiol.*, 1935, *16*, 191–203.

The author describes a method for the accurate measurement of the proteolytic activity of tissues, particularly epithelial tissues, cultivated in vitro. The method is based on the changes in transparency due to proteolysis brought about in thin sheets of coagulated egg albumin upon which the tissues are cultivated. Arithmetical values of the change in transparency are obtained photometrically from a series of photographic plates of the sheets of egg albumin. The sources of error in the method are discussed and one example of its use is described.—*Audrey G. Morgan.*

Sievert, Rolf M. Erd-γ-Strahlung und Ultrastrahlung. (Gamma radiation and ultra-radiation from the earth.) *Acta radiol.*, 1935, *16*, 155–168.

It is known that there is a natural radiation from the earth's surface made up of two qualities of rays—hard gamma radiation and so-called ultra-radiation. The author reviews the history of the demonstration of this fact and the research work that has been done to determine the nature of this radiation and

whether or not it has any biological effects. Experiments made at the Radiumhemmet in screening off this radiation and studying the germination and growth of seeds when screened and not screened seemed to show that the radiation stimulates germination and inhibits growth. These are preliminary experiments, however, and it will require much more extensive work before any definite conclusions can be reached. Moreover, the fact that the effects observed are slight does not prove that they are so in nature; for in the experiments the radiation acts only for a short time while under natural conditions it is acting continuously.—*Audrey G. Morgan.*

OVERGAARD, KRISTIAN. Experimentelles über kombinierte Wärmeröntgentherapie bösartiger Tumoren. (Experiments in combined heat and roentgen therapy of malignant tumors.) *Acta radiol.*, 1935, *16*, 461.

Experiments on white mice are described in which a combined diathermy and roentgen treatment was given. In one series of animals the roentgen therapy was given first and in another the diathermy was given first and the roentgen therapy afterward. Other series were given roentgen treatment alone and diathermy alone. The animals that were given combined treatment showed better therapeutic results than those treated with either method alone. It was possible to cure tumors with subtherapeutic doses of the two agents when both were used. In this way the injurious effects on the normal tissues of either agent when used alone could be avoided. The results seemed to be rather better in the series in which roentgen treatment was given first than in the one in which diathermy was given first. This may have been due to other factors, however, and the difference was not decided enough to prove a real superiority of this sequence.

The author believes the method may prove of clinical value after further testing on animals.—*Audrey G. Morgan.*

ENGELSTAD, ROLF BULL, and MOXNES, N. H. Untersuchungen über die möglichen biologischen Wirkungen der kosmischen Strahlung. (Study of the possible biological effects of cosmic radiation.) *Acta radiol.*, 1935, *16*, 485–497.

Experiments are described which were made on white mice with a view to determining the biological effects of cosmic rays. The experimental animals were kept in a pit 350 meters below the surface of the ground so that no cosmic radiation reached them (total ionization 4.63 I). The control animals were kept in a cellar outside the pit exposed to cosmic radiation (total ionization 8.58 I).

No difference could be seen in the general health of the experimental and control animals while alive and no differences were found on autopsy. Roentgen examination of the skeletons showed no differences. The only noticeable difference was that the average weight of the animals in the pit was greater than that of the animals in the cellar. There was a difference of almost 2 grams. It seems probable, therefore, that cosmic rays inhibit growth or the biological functions which result in growth. —*Audrey G. Morgan.*

ÅKERLUND, ÅKE. Strahlenschutz der jetzigen Schwedischen Durchleuchtungsgeräte. (Protection from the rays of the present Swedish roentgenoscopy apparatus.) *Acta radiol.*, 1935, *16*, 379–389.

The means of protection against the action of the rays from roentgenoscopy apparatus may be divided into protective arrangements forming a part of the apparatus and protective rules to be observed by the individual. Of the former the methods of primary protection consist of filtration and a primary cone with a variable opening. Secondary protection is furnished by large fluoroscopy screens, head protector, wing-shaped arm shields, bowl-shaped hand shields, lead gloves, protective stool, protective table, foot shields.

For individual protection the entire personnel should be in the safety room during the exposures. Continuous control of the protective apparatus is advisable with the fluorescent screen test and the blood of the operator should be examined periodically. The personnel should not work more than a few hours a day and should have six to eight weeks' vacation a year, one period in the summer and one in the winter. Strict measures for the control of the protective arrangements in the different Swedish roentgen services by the method of Sievert's condensation chamber have shown that the daily dose on various parts of the roentgenoscopist's body is considerably less than 0.2 r per day which is generally accepted as harmless.—*Audrey G. Morgan.*